

P020014/A

Conceptus.

October 17, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

FDA/CDRH/OCE/PMO
2002 OCT 18 P 2:11
RECEIVED

RE: Amendment to PMA No. P020014
Post-Approval Study Protocols
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

This PMA Amendment is to provide the final protocols, statistical analysis plans, and case report forms for the two post-approval studies of the Essure System.

Exhibit A provides the protocol, statistical analysis plan, and case report forms for the post-approval study of the 5-year follow-up of the Phase II and Pivotal trial participants.

Exhibit B provides the protocol, statistical analysis plan, and case report forms for the post-approval study of placement rates among newly trained physicians in the commercial setting.

Please let me know if you have any questions regarding this PMA Amendment. I can be reached at ((b) (6) | (b) (6)), or by fax at (b) (6), or by e-mail at (b) (6). Thank you for your continued review of this PMA application.

Sincerely,

(b) (6)

Attachments: Exhibit A and B

PMA Amendment: Post-Approval Study Protocols
October 17, 2002
P020014

SPF 1

**Post-Approval Study of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials**

(IDEs: G980152 and G000055)

**Conceptus Research Protocol
Essure 5-Year**

**Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070
U.S.A.
Telephone: (b) (6)
Fax: (650) 610-8363**

REVISION HISTORY

Original Protocol, Rev 00

10/17/02

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Appendix A: Statistical Analysis Plan

Appendix B: Case Report Forms

- Pivotal Trial
- Phase II Study
- Histology

1. TITLE

“Post-approval study of the Essure System: 5 Year Follow-up under Phase II and Pivotal Trials.”

2. PURPOSE OF STUDY

The purpose of this study is to demonstrate the long-term safety and effectiveness of Essure in providing permanent contraception.

3. STUDY DESIGN

This protocol combines the long-term follow-up already planned under the Phase II (Conceptus protocols #STOP 07/10; IDE #G980152) and Pivotal trials (Conceptus protocol #STOP 2000; IDE #G000055). Specifically, study participants implanted with at least one Essure Micro-insert will be followed annually for 5 years.

Findings from the U.S. Collaborative Review of Sterilization (CREST¹ study) will be used as a qualitative assessment.

Reference

1. Peterson HB, Xia Z, Hughes JM, et al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-1170

4. STUDY PLAN

Study participants who received implantation with at least one Essure Micro-insert in the Phase II or Pivotal trials of the Essure System (gamma design) will be followed for 5 years. Participants who are not relying on Essure for contraception will be followed for safety evaluation only, at 2, 3, 4, and 5 years after implantation. Participants who are relying on Essure for contraception will be followed for safety and effectiveness evaluation at 2, 3, 4, and 5 years after discontinuation of alternative contraception. The Pivotal trial and Phase II protocols also include an 18 month follow-up visit for study participants who are relying on Essure for contraception. However, since this post-approval study protocol is intended to provide *annual* effectiveness rate information, the 18-month visit will not be included in this protocol. The data from the 18-month visit will instead be reported in the IDE annual progress reports. Participants terminated from the Phase II or Pivotal trial due to lack of Micro-insert placement,

Micro-insert explantation, or who have become lost-to-follow-up in those studies, will not be followed under this protocol.

5. PRIMARY AND SECONDARY ENDPOINTS

5.1 The primary endpoints for the study are as follows:

1. Prevention of pregnancy for 5 years,
2. Safety of device wearing for 5 years

Pregnancy prevention will be determined by a pregnancy test at the 2 and 5 year follow-up visits and by phone assessment at the 3 and 4 year follow-up visits. Safety of device wearing will be evaluated by recording adverse events at each of the scheduled follow-up visits.

5.2 The secondary endpoint for the study are as follows:

1. Participant satisfaction with device wearing for 5 years,

Participant satisfaction with device wearing will be evaluated by participant interviews at scheduled follow-up visits.

6. INVESTIGATORS AND QUALIFICATIONS

The Investigators who participated in the Phase II and Pivotal trials will be the same Investigators who participate under this post-approval study protocol.

7. STUDY POPULATION

Study participants will be women who received implantation of at least one Essure Micro-insert in the Pivotal trial and participants in the Phase II trial that received at least one Micro-insert and agreed to be followed for 5 years¹.

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This study will not include those women terminated from the Phase II or Pivotal trials.

8. STUDY PROCEDURES

The case report forms for this study are included in **Appendix B**. These case reports forms are the same as currently used in the Phase II and Pivotal trials, with the addition of the case report forms that will be used for histology results (which are the same as those used in the pre-hysterectomy study of Essure; G960206).

All study procedures will be paid for by the Sponsor.

9.1 Follow-up Visits and Phone Contact

A description of each visit and phone contact is provided below.

- 9.1.1 Phone contact will be scheduled at three and four years following discontinuation of alternative contraception.
- 9.1.2 Office visits will be scheduled two and five years following discontinuation of alternative contraception.
- 9.1.3 Any participant who has had one or more Essure devices implanted, but is not able to rely on the device(s) for contraception, for any reason, will be followed at the 2, 3, 4 and 5 year follow-up time points (post-device placement) for safety and participant tolerance to device wearing. This includes participants who have had incisional sterilization, subsequent to Essure Micro-insert placement but without Micro-insert removal.
- 9.1.4 Additional office visits required for the investigation or management of an adverse event(s) must be recorded on the "Unscheduled Visit" Case Report Form.

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9.4 Intrauterine Procedures Post-Essure Placement

Participants will be instructed to contact the Investigator if they are scheduled to undergo any intrauterine procedure such as endometrial biopsy, dilatation and curettage (D&C), or hysteroscopy (diagnostic or operative) including endometrial ablation or resection. If such a procedure(s) is scheduled, the Investigator should inform the physician who will be conducting the procedure that there may be risks associated with the presence of the Essure Micro-inserts that, at this time, have not been identified. In the event of a hysteroscopic procedure, the Investigator will request the physician to make an evaluation of the tissue surrounding any portion of the Essure Micro-insert trailing into the uterine cavity and to provide photos and video footage when possible.

9.5 Extirpative Surgery of Reproductive Organs Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any extirpative surgery of the reproductive organs (hysterectomy, salpingectomy, oophorectomy), *for any reason*, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes and provide photos and video footage when possible. In the event that the extirpative surgery occurs in a participant whose devices were known to be located in her peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the

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location of the device, a determination as to whether the device(s) were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s). The search for the device should be limited to 30 minutes, and any free-floating devices should be retrieved and returned to Conceptus. The Investigator should obtain the excised fallopian tubes, when possible, and send them to Conceptus for histological evaluation. In any case, histology specimens retrieved should be evaluated and results forwarded to the Investigator and Conceptus. When the tubes are sent to Conceptus for evaluation, the case report forms attached as Appendix B will be used. If the participant is scheduled to undergo any intrauterine sampling procedure (D&C, endometrial biopsy), histology results should also be forwarded to the Investigator and Conceptus.

9.6 Transabdominal Surgery Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any surgery in the peritoneal cavity that would permit visualization and evaluation of the fallopian tube exterior, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes, and provide photos and video footage when possible. In the event that the surgery occurs in a patient whose devices were known to be located in the peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the location of the device, a determination as to whether the devices were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s).

10 ADVERSE EVENTS

Adverse events are defined as any untoward deviations in subject health away from baseline. Investigators must record and document all adverse events in the case report form, and record and report any unanticipated device related adverse effects to Conceptus and the reviewing IRB / Ethics Committee as soon as possible but no longer than 5 working days after becoming aware of the event. Unanticipated adverse device effect means any serious adverse effect on health or safety, or any life-threatening problem or death caused by or associated with a device, *if* that effect, problem or death was not previously identified in nature,

severity or degree of incidence in the investigational plan *or* any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. For all serious adverse events, the Investigator will send to Conceptus all appropriate paperwork (discharge summaries, office notes, etc.) that might be pertinent.

11 RECORDS AND REPORTS

11.1 Each Investigator will maintain the following accurate, complete and current records relating to the Investigator's participation in an investigation:



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15. DATE OF COMMENCEMENT

The proposed date of commencement for this post-approval study plan is immediately upon PMA approval.



Appendix A
STATISTICAL ANALYSIS PLAN

Post-approval study of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials
(IDEs: G980152 and G000055)

Conceptus Research Protocol
Essure 5-Year

Statistical Plan Summary

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Bayesian Perspective

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³ <http://www.mrc-bsu.cam.ac.uk/bugs/welcome.shtml>

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Determining Cumulative Failure Rates

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Age Adjustment

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Conservative Age Adjustment With Zero Failures

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Figure 1

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Appendix B

CASE REPORT FORMS

- 1. Pivotal Trial (STOP 2000)**
- 2. Phase II Study (STOP 07/10)**
- 3. Histology**

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Essure™ System
US Post-Approval Study for Newly Trained Physicians

October 17, 2002

Conceptus Protocol:
Essure PAS Placement

Sponsor:

Conceptus Incorporated
1021 Howard Avenue
San Carlos, CA 94070

Telephone 650-628-4700

Fax 650-802-2890

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REVISION HISTORY

Version 01

October 17, 2002

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1. Title
2. Study Purpose
3. Study Design
4. Primary Endpoints
5. Designated Person
6. Inclusion and Exclusion Criteria
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9. Records and Reports
10. Statistical Analysis and Reporting of Results
11. Financial Issues
12. Study period

Appendices

- A. Case Report Forms**
- B. Statistical Analysis Plan**

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1. Title

The title of this study is “Essure™ System US Post-Approval Study for Newly Trained Physicians”.

2. Study Purpose

The purpose of the Plan is to assess the bilateral placement rate in the commercial setting in newly trained physicians. The purpose is also to gather additional data regarding placement failure, to determine if there are any common characteristics that can be useful in future patient selection.

3. Study Design

This study is designed to collect demographic and micro-insert placement data on a total of 800 women from 40 physicians in the commercial setting in whom an Essure System is placed through the operating channel of the hysteroscope. Data will also be collected on women in whom the procedure is begun, but in whom an Essure System is not placed through the operating channel of the hysteroscope (“non-attempts”), but this is in addition to the 800 women in whom there is an attempt at placement with Essure.

Although only 40 physicians are needed to reach a total of 800 women, 45 physicians will be enrolled in this study in the event that not all physicians complete a total of 20 cases, or do so on a timely basis. Enrollment in this study will cease after data is available from 40 physicians who have provided data regarding 20 cases of Essure placement attempt.

Physician enrollment in this study will be limited to no more than 6 physicians from any one state, and no more than 2 physicians from any one institution. In

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addition, no more than two-thirds of the physicians will represent either community-based hospitals or teaching institutions.

The first 45 physicians in major metropolitan areas in the United States who complete the didactic and model portions of the training program will be asked to participate in this study. Such physicians will be enrolled in the study only if: 1) they agree to participate, and 2) they do not have previous experience in Essure micro-insert placement. In addition, they will not contribute cases to this study until after they have completed the preceptoring portion of the training program.

The enrolled physicians will then collect demographic and micro-insert placement data on the first cases performed after preceptoring is complete, until placement data are available on a total of 20 women in whom an Essure System was placed through the operating channel of the hysteroscope. Since data on "non-attempts" will also be collected, it is anticipated that more than 800 women will be enrolled in order to obtain data on 800 women with an actual placement attempt.

Physicians enrolled in this study will include the following statement in their informed consent of the patient:

"I agree to participate in the Postmarket Surveillance Study being conducted on the Essure System. I acknowledge that there is no benefit to me for participating in this study. I agree to allow information about me and my placement procedure to be shared with the Sponsor, Conceptus, its employees and consultants, and the FDA. I understand that the information sent to the Sponsor and the FDA will not identify me, but that Conceptus or the FDA may have reasons to review identifiable information about me in the office of my physician."

4. **Primary Endpoints**

The primary endpoints are as follows:

1. Bilateral micro-insert placement rate, and
2. Identification of factors predictive of micro-insert placement failure

Some women may not achieve bilateral placement until after two micro-insert placement procedures. This study will only incorporate placement data from the 1st micro-insert placement procedure for each patient. So, if a patient receives unilateral placement during the first placement procedure and an Essure micro-insert is successfully placed in the contralateral tube during the second placement procedure, then the placement status for such a patient under this study would be “unilateral placement”, even though bilateral placement was eventually achieved.

Bilateral micro-insert placement success or failure will be noted on the Case Report Forms (CRFs) for the first placement procedure for a given patient. The following demographic information will also be collected on the CRFs to determine if any of these variables are predictive factors for placement failure:

- race
- age
- education level
- weight
- height
- income
- gravidity
- parity
- number of vaginal births
- number of abortions
- history of PID/salpingitis
- history of prior abdominal/pelvic surgery

- unusual uterine anatomy (unicornuate uterus, bifurcated uterus)
- other remarkable obstetric or gynecological history
- body mass index
- contraceptive method used just prior to Essure placement procedure
- time in menstrual cycle when Essure placement procedure was performed
- whether the patient received hormonal manipulation to promote atrophic or proliferative endometrium prior to placement procedure

In addition, the level of prior hysteroscopic experience of the physician and certain procedure details (equipment, distension, anesthesia method, etc.) will be recorded.

5. Designated Person

The Director of Professional Education at Conceptus will be responsible for execution of this study, and the V.P. of Clinical Research and Medical Affairs will be responsible for the data analysis and report preparation.

6. Inclusion and Exclusion Criteria

All inclusion and exclusion criteria from the Instructions for Use approved under the PMA will apply.

Additional inclusion criteria:

- Women who are willing to allow their data to be shared with the Sponsor and the FDA.

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7. Data collection

Data will be collected using standardized Case Report Forms (CRFs). The Physician or his/her designee will enter the relevant information into electronic case report forms. The questions to be incorporated into the electronic CRFs for this study are attached as **Appendix A**.

No patient follow-up will be conducted as part of this study, with the exception of data from follow-up HSGs performed to evaluate the reasons for placement failure in women who desire a second attempt at device placement (although, as stated above, the data from the second attempt will not be recorded under this protocol).

8. Instructions for Use

Micro-insert placement will be performed according to the Instructions for Use (IFU) approved under the Essure PMA (P020014).

9. Records and Reports

Records

The following records will be maintained by Conceptus during the course of this study, and for two years after acceptance of the final study report by the FDA:

- All correspondence with the physicians or FDA regarding this study, including required reports,
- Signed agreements from each of the Physicians, stating the commitment to conduct the study in accordance with the approved protocol,
- The approved protocol, with documentation of the date and reason for any deviation from the protocol, and
- All data collected and analyses conducted in support of the study.

The following records will be maintained by the Physician during the course of the study, and for two years after acceptance of the final study report by the FDA:

- All correspondence between physicians, FDA, and Conceptus regarding this study and any data collected as part of the study
- The approved protocol, with documentation of the date and reason for any deviation from the protocol
- All data collected under this study

Content and timing of reports

A final report will be submitted to FDA within 3 months of receipt of data regarding the 800th patient to undergo an Essure placement procedure under this study. It is anticipated that patient enrollment will be completed in approximately one year from study commencement. If enrollment takes longer than planned, an interim report will be submitted one year from the date of commencement of the study, to be followed with a final report on all patients.


The report(s) will include the information relating to the bilateral placement rates of newly trained commercial physicians as well as an analysis of factors that may impact bilateral placement (see Section 4 above for a list of these potential factors).

10. Statistical Analysis and Reporting of Results

The Statistical Analysis Plan is attached as **Appendix B**.

11. Financial Issues

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12. Study period

The study is anticipated to commence within 2 months of PMA approval, and is expected to be approximately 12 months in duration.

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Appendix A

Case Report Forms

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Appendix B
Statistical Analysis Plan

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¹ <http://ftp.sas.com/techsup/download/stat/glmm800e.html>

² <http://www.mrc-bsu.cam.ac.uk/bugs/>

³ Calculations performed using PASS (Power Analysis and Sample Size), <http://www.ncss.com/pass.html>

Post-Approval Study

Placement Rates in Newly Trained Physicians

October 17, 2002

Page 19 of 20

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OB
1030a 5/7/2002 REC

DOCUMENT # P020014 ^{A001} SUPPLEMENT # A1

510(k) 60th DAY: _____ PMA 45TH DAY: _____
510(k) 90th DAY: _____ PMA 90TH DAY: _____
PMA 180TH DAY: _____

conceptus

REVIEWER: (b) (6) _____

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COMMENTS:

1030a 5/7/2002 RSN

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PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A001 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.

SHORT NAME CONCEPTUS

CONTACT (b) (6)

DIVISION _____

ADDRESS 1021 HOWARD AVE.

SAN CARLOS, CA 94070

PHONE NO. (650) 802-7240

FAX NO. (650) 610-8363

MANUFACTURER CONCEPTUS, INC.

REG NO. 2951250

(b) (4)

(b) (6), (b)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 02-MAY-2002

CYCLE # 1

DATE RECEIVED IN ODE 03-MAY-2002

CYCLE START 22-APR-2002

DATE FILING DUE 06-JUN-2002

ELAPSED

LAST CYCLE

DATE DECISION DUE _____

FDA TIME 11

11

MFR TIME 0

0

**DRAERD REVIEWER RECORD FOR ORIGINAL 510(K)s,
AND PMA AND IDE SUPPLEMENTS**

Document No. _____ Reviewer _____ Date Assigned _____

CONSULTING REVIEWS DESIGNATED, AS APPROPRIATE, BY BRANCH CHIEF AND LEAD REVIEWER, AT THE BEGINNING OF THE REVIEW:

<u>SPECIALTY</u>	<u>REVIEW NEEDED?</u>		<u>REVIEWER</u>	<u>DATES</u>	
	YES	NO		SENT	RETURNED
CLINICAL	_____	_____	_____	_____	_____
ENGINEERING/ PHYSICS	_____	_____	_____	_____	_____
CHEMISTRY/ BIOMATERIALS	_____	_____	_____	_____	_____
SOFTWARE	_____	_____	_____	_____	_____
IMMUNOLOGICAL/ STERILITY	_____	_____	_____	_____	_____
TOXICOLOGY/ BIOCOMPATIBILITY	_____	_____	_____	_____	_____
STATISTICS	_____	_____	_____	_____	_____
OTHER _____	_____	_____	_____	_____	_____

COMMENTS:

**REVISED 1/2/96 LMS
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QUALITY CONTROL OVERVIEW OF DOCUMENT

A. ASSOC. DIRECTOR QC OVERVIEW: MEDICAL QC OF SUBMISSION IS NECESSARY?

YES _____ NO _____ INITIALS/DATE _____

B. IF YES IS NOTED ABOVE, MEDICAL OFFICER QC OVERVIEW:

1. Examination of the specialty reviews indicate there are remaining clinical issues that should be addressed (See attached sheet for summary).

INITIALS/DATE _____

2. In my opinion, all pertinent clinical issues have been adequately addressed.

FINAL SIGNOFF: MEDICAL OFFICER/DATE _____

FINAL SIGNOFF: ASSOC. DIRECTOR/DATE _____

REVISED: 1/2/96 LMS
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

May 03, 2002

(b) (6)
CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A001
Dated: 02-MAY-2002
Received: 03-MAY-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (b) (6). All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

(b) (6)

Center for Devices and
Radiological Health

PO20014

PMA/Module V/A1
Conceptus, Inc.

Allez VI

Conceptus.

May 2, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Conceptus Essure™ System for Permanent Birth Control
Corrections to Phase II Study Report
PMA Shell Number: M010031- Module V/Amendment 1

Dear (b) (6) :

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FDA/CDRH/OCE/

(b) (4)



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We apologize for these errors and regret any inconvenience they have caused. If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, or at (b) (6) via e-mail.

Sincerely,

(b) (6)



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J. Safety/Comfort of Micro-insert Wearing

Micro-insert Wearing Data

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K. Effectiveness

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P020014/A2

Module IV/A1
Conceptus, Inc.

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Conceptus®

May 15, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Conceptus Essure™ System for Permanent Birth Control
Amendment to Extend Shelf Life
PMA Shell Number: M010031- Module IV/Amendment 1

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MAY 15 11 29 AM '02

FDA/CDRH/OCE/DMC

Dear (b) (6) :

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If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, or at (b) (6) via e-mail.

Sincerely,

(b) (6)

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VP-0212.PV Rev. 2

**1 Year and 2 Year Accelerated Aging Study Protocol
for the Essure (STOP) System**

APPROVALS:

(b) (6)



2/22/02

Date

2/28/02

Date

2/13/2002

Date

2/13/2002

Date

2/19/02

Date

Rev. 2	VP-0212.PV 1 Year and 2 Year Accelerated Aging Study Protocol for the Essure (STOP) System	Page 1 of 8
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VR-0212.PV

**Accelerated Aging Study
for the Essure (STOP) System
2 Year Final Report**

APPROVALS:



5/2/02
Date

5.6.02
Date

5/2/02
Date

5-3-2002
Date

5/6/02
Date

Rev. 1	VR-0212.PV Accelerated Aging Study for the Essure (STOP) System 2 Year Final Report	1 of 11
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APPENDIX I

VIBRATION CONTROL SPECTRA

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APPENDIX II

SEAL STRENGTH DATA

(b)(4)

P020014/A3/C/

PMA/Module V/A2
Conceptus, Inc.

Conceptus

May 24, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Conceptus Essure™ System for Permanent Birth Control
Correction to Phase II Study Report
PMA P020014 - Module V/Amendment 2

RECEIVED
MAY 28 11 42 AM '02
FOIA/CDRH/ISSR/SMC

Dear (b) (6):

This is to inform you of an error in the Phase II Study Report submitted as part of Module V on April 9, 2002. The error is contained on page 000157 (refer to page-stamped numbers) of Exhibit F: Study Deviations, Table 1. Deviation Report (Volume 1 of 3). The error is discussed below, and the corrected page is attached for your reference.

Page 000157 – Exhibit F: Study Deviations, Table 1

The number of deviations reported under the heading of “Follow-up Schedule Deviations” (Table 1) was 34, however the actual number described in the corresponding text was 42. Although all of the deviations were described in the text following the table, the table had an incorrect tally of the deviations. We have also corrected the total number of deviations accordingly.

We apologize for this error and regret any inconvenience this has caused. If there are questions regarding this submission, please contact me at (b) (4), (b) (6) } via telephone, (b) (6) } via fax, or at (b) (4), (b) (6) } via e-mail.

Sincerely,

(b) (6)

[Redacted signature block]

1

STUDY DEVIATIONS

(b) (4)



LOT

PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A004 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.

SHORT NAME CONCEPTUS

CONTACT (b) (6)

DIVISION _____

ADDRESS 1021 HOWARD AVE.

SAN CARLOS, CA 94070

PHONE NO. (650) 802-7240

FAX NO. (650) 610-8363

MANUFACTURER CONCEPTUS, INC.

REG NO. 2951250

(b) (6)

(b) (6)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 05-JUN-2002

CYCLE # 1

DATE RECEIVED IN ODE 07-JUN-2002

CYCLE START 22-APR-2002

DATE FILING DUE _____

ELAPSED

LAST CYCLE

DATE DECISION DUE _____

FDA TIME 46

46

MFR TIME 0

0

AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
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C001	<u>FILE</u>	<u>22-APR-2002</u>	
A001	<u>UMIN</u>	<u>03-MAY-2002</u>	
A002	<u>UMIN</u>	<u>16-MAY-2002</u>	
A003	<u>UMIN</u>	<u>28-MAY-2002</u>	

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

June 07, 2002

(b) (6)

CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A004
Dated: 05-JUN-2002
Received: 07-JUN-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (301)594-5072. All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

(b) (6)

Center for Devices and
Radiological Health

JUN - 7 2002

CDRH SUBMISSION COVER SHEET				
Date of Submission: June 5, 2002			FDA Document Number: PMA P020014	
Section A Type of Submission				
PMA	PMA Supplement	PDP	510(k)	Meeting
<input type="checkbox"/> Original submission <input type="checkbox"/> Modules submission <input checked="" type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	<input type="checkbox"/> Regular <input type="checkbox"/> Special <input type="checkbox"/> Panel Track <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA Supplement	<input type="checkbox"/> Presubmission summary <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of intent to start clinical trials <input type="checkbox"/> Intention to submit Notice of Completion <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated <input type="checkbox"/> Additional information <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated	<input type="checkbox"/> Pre-IDE meeting <input type="checkbox"/> Pre-PMA meeting <input type="checkbox"/> Pre-PDP meeting <input type="checkbox"/> 180-day meeting <input type="checkbox"/> Other (specify):
IDE	Humanitarian Device Exemption	Class II Exemption	Evaluation of Automatic Class III Designation	Other Submission
<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	Describe submission:
Section B Applicant or Sponsor				
Company / Institution name: Conceptus Incorporated		Establishment registration number: 2951250		
Division name (if applicable): Not Applicable		Phone number (include area code): (650) 802-7240		
Street address: 1021 Howard Avenue		FAX number (include area code): (650) 802-2890		
City: San Carlos	State/Province: CA 94070	Country: USA		
Contact name: (b) (6)				
Contact title: (b) (6)		Contact e-mail address: (b) (6)		
Section C Submission correspondent (if different from above)				
Company/Institution name: Same as above		Establishment registration number: Same as above		
Division name (if applicable): Same as above		Phone number (include area code): (b) (6)		
Street address: Same as above		FAX number (include area code): Same as above		
City: Same as above	State/Province: Same as above	Country: Same as above		
Contact name: Same as above				
Contact title: Same as above		Contact e-mail address: Same as above		

Section D1	Reason for Submission - PMA, PDP, or HDE	
<input type="checkbox"/> New device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or expanded indications <input type="checkbox"/> Licensing agreement <input type="checkbox"/> Process Change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Sterilization <input type="checkbox"/> Packaging <input type="checkbox"/> Other (specify below) <input type="checkbox"/> Response to FDA correspondence: <input type="checkbox"/> Request for applicant hold <input type="checkbox"/> Request for removal of applicant hold <input type="checkbox"/> Request for extension <input type="checkbox"/> Request to remove or add manufacturing site <input checked="" type="checkbox"/> Other reason (specify): update clinical data	<input type="checkbox"/> Change in design, component, or specifications: <input type="checkbox"/> Software <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (specify below) <input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager <input type="checkbox"/> Distributor <input type="checkbox"/> Report submissions: <input type="checkbox"/> Annual or periodic <input type="checkbox"/> Post-approval study <input type="checkbox"/> Adverse reaction <input type="checkbox"/> Device defect <input type="checkbox"/> Amendment <input type="checkbox"/> Change in ownership <input type="checkbox"/> Change in correspondent
Section D2	Reason for Submission - IDE	
<input type="checkbox"/> New device <input type="checkbox"/> Addition of institution <input type="checkbox"/> Expansion/extension of study <input type="checkbox"/> IRB certification <input type="checkbox"/> Request hearing <input type="checkbox"/> Request waiver <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of application <input type="checkbox"/> Unanticipated adverse effect <input type="checkbox"/> Notification of emergency use <input type="checkbox"/> Compassionate use request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continuing availability request <input type="checkbox"/> Other reason (specify):	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent <input type="checkbox"/> Design <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing process <input type="checkbox"/> Protocol - feasibility <input type="checkbox"/> Protocol - other <input type="checkbox"/> Sponsor <input type="checkbox"/> Report Submission: <input type="checkbox"/> Current investigator <input type="checkbox"/> Annual progress <input type="checkbox"/> Site waiver limit reached <input type="checkbox"/> Final	<input type="checkbox"/> Response to FDA letter concerning: <input type="checkbox"/> Conditional approval <input type="checkbox"/> Deemed approved <input type="checkbox"/> Deficient final report <input type="checkbox"/> Deficient progress report <input type="checkbox"/> Deficient investigator report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request extension of time to respond to FDA <input type="checkbox"/> Request meeting
Section D3	Reason for Submission - 510(k)	
<input type="checkbox"/> New device <input type="checkbox"/> Addition or expanded indications <input type="checkbox"/> other reason (specify):	<input type="checkbox"/> Change in technology <input type="checkbox"/> Change in design	<input type="checkbox"/> Change in materials <input type="checkbox"/> Change in manufacturing process

Section E Additional Information on 510(k) Submissions					
Product codes of devices to which substantial equivalence is claimed:				Summary of, or statement concerning, safety and effectiveness data:	
1	2	3	4	<input type="checkbox"/> 510 (k) summary attached <input type="checkbox"/> 510 (k) statement	
5	6	7	8		
Information on devices to which substantial equivalence is claimed:					
510(k) Number	Trade or proprietary or model name			Manufacturer	
1	1			1	
2	2			2	
3	3			3	
4	4			4	
5	5			5	
6	6			6	
Section F Product Information - Applicable to All Applications					
Common or usual or classification name: Device, Occlusion, Tubal, Contraceptive					
Trade or proprietary or model name			Model number		
1 Essure (formerly STOP Device) System			PCD 001/ ESS001		
2					
3					
4					
5					
FDA document numbers of all prior related submissions (regardless of outcome):					
1 G960052	2 G960206	3 G980152	4 G000055	5 G010223	6 I010191
7 M010031/I	8 M010031/II	9 M010031/III	10 M010031/IV	11 010031/V	12 P020014
Data included in submission : <input type="checkbox"/> Laboratory testing <input type="checkbox"/> Animal trials <input checked="" type="checkbox"/> Human trials					
Section G Product Classification - Applicable to All Applications					
Product code: KNH	C.F.R. section 884.5380		Device class: <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input checked="" type="checkbox"/> Class III <input type="checkbox"/> Unclassified		
Classification panel: Obstetrics/Gynecology					
Indications (From labeling): The Essure™ System is indicated for permanent birth control (female sterilization) by occlusion of the fallopian tubes.					

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.

FDA Document Number:

Section H Manufacturing/ Packaging / Sterilization Sites

<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number: 2951250	<input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/relabeler
--	---	--	---

Company/institution name: Conceptus Incorporated	Establishment registration number: 2951250
--	--

Division name (if applicable): Not Applicable	Phone number (include area code): (b) (6)
--	---

Street address: 1021 Howard Avenue	Fax number (include area code): (650) 802-2890
---	--

City: San Carlos	State/Province: CA	Country: USA	ZIP/Postal Code: 94070
-------------------------	---------------------------	---------------------	-------------------------------

Contact Name: **(b) (6)**

Contact Title: (b) (6)	Contact e-mail address: (b) (6)
-------------------------------	---

<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number: (b) (4)	<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input checked="" type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/ relabeler
--	---	---	---

Company/institution name: (b) (4)	Establishment registration number: (b) (4)
---	--

Division name (if applicable): N/A	Phone number (include area code): (b) (4)
---	---

Street address: (b) (4)	Fax number (include area code): (b) (4)
--------------------------------	---

City: (b) (4)	State/Province: (b)	Country: USA	ZIP/Postal Code: (b) (4)
----------------------	----------------------------	---------------------	---------------------------------

Contact Name: **(b) (4)**

Contact Title: Validation Coordinator	Contact e-mail address:
--	-------------------------

<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number:	<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/ relabeler
---	--	---	--

Company/institution name:	Establishment registration number:
---------------------------	------------------------------------

Division name (if applicable):	Phone number (include area code): ()
--------------------------------	--

Street address:	Fax number (include area code): ()
-----------------	--

City:	State/Province:	Country:	ZIP/Postal Code:
-------	-----------------	----------	------------------

Contact Name:

+Contact Title:	Contact e-mail address:
-----------------	-------------------------

Conceptus®

June 5, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Amendment to PMA No. P020014
Additional One-year Data
Conceptus Essure™ System for Permanent Birth Control


Dear (b) (6) :

(b) (4)



One-Year Follow-up Status: Pivotal Trial Women with Bilateral Placement

(b)(4), (b)(6)



July PMA Amendment

(b) (4)



Identification of Updated Items

(b) (4)



(b) (4)



(b) (4)



If you have any questions regarding this supplement, I can be reached at (b) (6) or by fax at (b) (6), or by e-mail at (b) (6). In addition, you may contact (b) (6) at (b) (6), by fax at (b) (6), or by e-mail at (b) (6). Thank you for your continued review of this PMA application.

Sincerely,

(b) (6)



Table A. One-year Follow-up Status: Pivotal Trial Women with Bilateral Placement

STATUS	NUMBER
(b) (4)	

Table B. Due Dates for Pivotal Trial Women Not Yet Completing One-year Visit, N=27 (26 not yet due + 1 due but visit not completed prior to database freeze)

Patient No.	One-year Visit <i>Due Date</i> (2002)	Monthly Totals
-------------	--	----------------

(b) (4), (b) (6)




Table C. Pivotal Trial Women Currently Lost-to-Follow-up, n=17

Patient No.	Last Follow-up Visit Completed	Total From Each Visit
(b) (4), (b) (6)		

Conceptus Essure™ System

Amendment to PMA No. P020014

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**Volume 3 – PER FDA REQUEST, NOT RECOPIED FOR THIS
AMENDMENT. PLEASE REFER TO VOLUME 3 OF APRIL 19, 2002
PMA FOR THE BELOW DOCUMENTS**

- Exhibit A - Study Protocol
- Exhibit B - Informed Consent Form
- Exhibit C - Statistical Plan (Final Clean Copy)
- Exhibit D - Statistical Plan (with Changes Noted)

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- Exhibit A - Patient Questionnaires
- Exhibit B - Electronic Case Report Forms

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- Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

(b) (6)



(b) (6)



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Summary Data Tables:

- Number 1 -** Patient Enrollment and Reasons for Discontinuation
- Number 2 -** Months of Wearing
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- Number 9 -** HSG Results for Unsuccessful Placement
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- Number 17 -** 6 Month PAC Phone Contact
- Number 18 -** One-year PAC Office Visit
- Number 19 -** Adverse Events
- Number 20 -** Investigator reliance by country

Volume 11

References for Pivotal Trial Report

PMA
Conceptus, Inc.

Volume 12 - *Updated*

Proposed Labeling (Product, Patient, Professional)

Professional Training Program

Summary of Safety and Effectiveness

2012 - 1 - 100

Conceptus Essure™ System

Amendment to PMA No. P020014

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PMA
Conceptus, Inc.

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(b) (6)



(b) (6)



Volumes 8-10

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PMA
Conceptus, Inc.

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Proposed Labeling (Product, Patient, Professional)

Professional Training Program

A

Section I. Clinical Data Report: Pivotal Trial

A. Executive Summary

Introduction

Provided in this introductory section is a description of the unintended pregnancy and abortion rates in the United States as well as the complications associated with pregnancy, the documented need for contraceptive alternatives, a discussion of the risks associated with current methods of permanent birth control (female sterilization), and the unique characteristics of the Essure System for Permanent Birth Control.

Unintended Pregnancy/Abortion Rates

Unintended pregnancy is a significant public health issue that affects not only the woman involved, but also society as a whole. The significance of this public health need is evidenced by the signing into law of Title X of the Public Health Service Act, which provides for a comprehensive federal program devoted entirely to providing family planning services on a national basis.

Using data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, it has been estimated that almost half (48%) of all pregnancies in the United States in 1994 were unintended, and 54% of these ended in abortion¹. In 1994 alone, there were an estimated 3,000,000 unintended pregnancies, with an estimated half (48%) of women aged 15-44 having had at least one unplanned pregnancy sometime in their lives¹. Although teenagers have the highest rate of unintended pregnancy,

¹ Henshaw SK. Unintended Pregnancy in the United States. *Family Planning Perspectives*, 1998, 30(1): 24-29 & 46.

the second highest rate is found in women aged 40-44². Furthermore, the rate of unintended pregnancies in the U.S. has declined little over the past several decades, and remains higher than other developed nations².

In 1997, over one million abortions were performed, and an estimated 43% of women will have at least one abortion by the time they are 45 years old¹.

Abortion is not just an issue that faces teenagers. In fact, based on a 1994-1995 national survey of almost 10,000 abortion patients, over 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women who were age 30 or over³.

Maternal Risks of Pregnancy

According to the CDC⁴, approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Two to three women die each day from a pregnancy-related complication, and the maternal mortality rate has not declined since 1982⁴. The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy. It should be noted that the risk of pregnancy-related death rises after the age of 35⁵. In addition to mortality resulting from pregnancy, the CDC states that more than one in three pregnant women in the U.S. develop a pregnancy-related complication⁴. The most common complications include: miscarriage, ectopic pregnancy, hemorrhage, infection, diabetes, high blood pressure, excessive vomiting, premature labor, need for Caesarean delivery, and depression. Furthermore, based on 1986-1987 data from the National Hospital Discharge Survey (NHDS), an estimated 22.2 per 100 hospitalizations involving a birth were non-delivery

² Global Health Options.

³ Henshaw SK. Abortion Patient in 1994-1995: Characteristics and Contraceptive Use. *Family Planning Perspectives*, 28: 140-147 & 158, 1996.

⁴ CDC's Reproductive Health Information Source. *Safe Motherhood: Promotion Health for Women Before, During, and After Pregnancy 2002*.

⁵ CDC Press Release: Fact Sheet, Pregnancy-Related Mortality.

related hospitalizations of pregnant women⁶. Hospitalization for a pregnancy-related complication required an average of >2 million hospital days of care per year and cost >1 billion dollars annually⁶. The authors of this study provided a nationwide estimation of serious pregnancy-related morbidity following childbirth: 62,400 readmissions occurred during the postpartum period, yielding an average annual rate of 8.1 readmissions per 1,000 deliveries.

As stated by the CDC, childbirth remains the most common reason for hospitalization in the U.S., and complicated pregnancies result in more costly hospitalizations. Thus, since women who have unintended pregnancies are less likely to have appropriate prenatal care, more likely to have entry into prenatal care at a later stage of the pregnancy, and are at an increased risk of domestic violence⁷, they are presumably at higher risk of complications and account for more costs related to pregnancies.

Risks to Infant/Child

The National Commission to Prevent Infant Mortality has stated that: “Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception.”⁸. Similarly, a review by the U.S. Institute of Medicine of the research on this topic concluded that “the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development⁹. The CDC also states that an infant from an unintended pregnancy has an increased risk of low birth rate, neonatal mortality, risk of SIDS, and developmental problems⁷.

Clearly, there is a significant public health issue represented by these facts and figures.

⁶ Franks AL. Hospitalization for pregnancy complications, United States, 1986 and 1987. *Am J Obstet Gynecol* 1992; 166:1339-44.

⁷ Koonin LM. Promoting Healthy Pregnancies: Counseling and Contraception. September 20, 2000.

⁸ Alan Guttmacher Institute. *Title X and the U.S. Family Planning Effort*.

⁹ Alan Guttmacher Institute. *Family Planning Improves Child Survival and Health*. 1998.

Need for Contraceptive Alternatives

Based on data from the 1995 National Survey on Family Growth, it has been suggested in the literature that the high rates of unintended pregnancy reflect dissatisfaction with current methods¹⁰. In addition, based on a 64-country survey, it has been shown that the prevalence of contraceptive use rises with increased access to a variety of contraceptive methods¹¹.

The 1995 National Survey on Family Growth provided data on the current profile of contraceptive use in the United States based on a survey of almost 7,000 women. The survey revealed that the percentage of women discontinuing contraceptive use for method-related reasons within 12 months of method initiation was 44%¹⁰. In addition, during the lifetime of a typical woman who uses reversible methods of contraception, she will discontinue use for a method-related reason 9.5 times. If women using sterilization are included as well, the typical woman will discontinue use of a contraceptive for a method-related reasons only 7.2 times during her lifetime. The survey also found that the typical woman will experience 1.8 unintended pregnancies. If women using sterilization are included as well, the typical woman will experience 1.3 unintended pregnancies. The survey also noted that 6% of sexually active women were not using a contraceptive, which translates to approximately 3.5 million women at risk of unintended pregnancy. Indeed, of the 6 million pregnancies that occurred that year, nearly half were unintended, and more than half of these unintended pregnancies occurred among women who were using contraceptives.

The need for contraceptive alternatives has been acknowledged in recent years not only in the published literature, but also at meetings of the FDA's OB/GYN

¹⁰ Trussel J. Contraceptive Failure, Method-Related Discontinuation and Resumption of Use: Results from the 1995 National Survey of Family Growth. *Family Planning Perspectives*, 1999, 31(2): 64-72 & 93.

¹¹ Ross J. Contraceptive Method Choice in Developing Countries. *International Family Planning Perspectives*, 2001, 28(1): 32-40.

Advisory Committee. Additionally, the need for less invasive transcervical methods of sterilization has been a primary research focus for the USAID Office of Population, Family Health International (FHI), the CONRAD Program, and the WHO Human Reproduction Program.

In introductory remarks to the panel convened in October of 1996 for the review of the PMA for the Lea's Shield, Mr. Pollard (Chief, Obstetrics and Gynecology Devices Branch, FDA) stated: "I would like to add at this point that FDA is responsive to the concerns of women's advocacy groups across the U.S. Many of these groups are very concerned about the limited number of contraceptive options available to women and believe that FDA should be re-examining its review standards for evaluation of these products. This need for more contraceptive options was most recently emphasized in the report that just issued from the Institute of Medicine entitled 'Contraceptive Research and Development: Looking to the Future', highlighting the high rate of unintended pregnancies in the U.S. and worldwide."

In addition, the FDA convened a meeting of the panel in October of 1999 to discuss the requirements for vaginal barrier contraceptive devices to "recalibrate our premarket entry process and optimize the balance of premarket and postmarket requirements" for these devices, as stated by Mr. Pollard. This was largely driven by the results of the 1995 National Survey on Family Growth. Mr. Pollard presented to the panel some of the results discussed above from the survey regarding high rates of unintended pregnancy, abortion, and discontinuation of contraception due to method-related reasons, and went on to state: "To us, at FDA, that describes a huge unmet need." While the focus of the panel meeting was for vaginal barrier contraceptive devices rather than tubal occlusion devices, the underlying motivation for convening the meeting still pertains to consideration of the Essure System: the large unmet need in the area of contraceptive alternatives for women.

The author of the published findings of the 1995 Survey concluded that the high pregnancy rates in the survey “do not reflect the inherent efficacy of methods when used correctly and consistently, but instead reflect imperfect use because most reversible methods are difficult to use correctly.” The author went on to state: “such high rates of discontinuation almost surely reflect dissatisfaction with current methods.”

Prevalence of Tubal Sterilization

Currently, women must choose between temporary reversible methods, with all the limitations discussed above, and permanent birth control (sterilization), with its attendant invasiveness, morbidity, and mortality. Discussed below is the prevalence of tubal sterilization as a contraceptive choice, as well as the risks associated with this method.

Tubal sterilization is the most prevalent method of birth control in the United States. From 1994-1996, more than 2,000,000 tubal sterilizations were performed, for an annual incidence of 11.5 per 1,000 women, or 684,000 per year¹². As noted by Dr. Carolyn Westhoff at a recent meeting on transcervical sterilization sponsored by ARHP, this may well be an underestimate due to the difficulty in capturing the data in recent years.

All currently approved methods of tubal sterilization require access to the peritoneal cavity, and therefore carry the inherent risk associated with invasive surgery. Half of the tubal sterilizations are performed immediately post-partum and are done via mini-laparotomy or laparotomy¹³. The other half represent “interval” sterilizations, 89% of which are done laparoscopically¹³. Therefore, a slight majority of tubal sterilizations are performed by mini-

¹² MacKay AP. Tubal Sterilization in the United States, 1994-1996. *Family Planning Perspectives*, 2001, 33(4):161-166.

¹³ ACOG Technical Bulletin #222 – April 1996. Sterilization.

laparotomy/laparotomy. Currently, laparoscopy is predominantly performed with general anesthesia and involves one or more punctures of the abdominal wall for insertion of a laparoscope; the tubal ligation procedure is then performed through the puncture sites in the abdomen. Both laparotomy and mini-laparotomy are more extensive procedures and require relatively longer recovery periods than laparoscopic methods. About 93 percent of the procedures in the U.S. are performed in a hospital or surgi-center under general anesthesia, with laparoscopic procedures requiring an average of 4-5 hours of hospital recovery time¹⁴, an average of 4-6 days before returning to regular activities, not including the day of surgery^{15,16}, and an average of 3 days before returning to work¹⁶. For procedures performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

Risks with Tubal Sterilization – Mini-Laparotomy/Laparotomy

The Centers for Disease Control and Prevention (CDC) CREST study¹⁸ reported on a subgroup of almost 300 women who underwent interval tubal sterilization by laparotomy. In this subgroup, a major complication rate of 5.7% was reported¹⁷, which was comprised of febrile morbidity and re-hospitalizations. Re-hospitalization occurred for the following reasons: pelvic abscess, pulmonary abscess, pulmonary embolus, bowel obstructions, staph wound infection at site of laparotomy incision, etc. The mean length of postoperative hospital stay was increased by 1.9 nights for women who had at least one complication as compared to those without complication¹⁷. This does not include the additional

¹⁴ Bordahl PE. Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study. *Obstet Gynecol* 1993; 81: 137-41.

¹⁵ Fraser RA. The prevalence and impact of pain after day-care tubal ligation surgery. *Pain* 39 (1989) 189-201.

¹⁶ Garcia FA. Economic and Clinical Outcome of Microlaparoscopic and Standard Laparoscopic Sterilization, A Comparison. *J Reprod Med* 2000; 45:372-376.

¹⁷ Layde PM. Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy. *Obstet Gynecol* 62:180, 1983.

¹⁸ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-70.

hospitalization experienced by women who were readmitted following their initial discharge. The mean total convalescence period from the time of the surgery until the resumption of normal activities was increased by 8.3 days (from 9.6 days) among women experiencing a complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparotomy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (1.8%), primary incision complications (12.6%), infections (1.1%), and "other" (3.3%). The total complication rate in this study, for the complications reported, was 18.8%. In a similar study comparing the Filshie Clip with the Tubal Ring under laparotomy²⁰, the following complications were noted: surgical injuries (7.3%), primary incision complications (13.9%), infections (0.9%), and "other" (1.4%). The total complication rate in this study, for the complications reported, was 23.5%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional approach.

Risks with Tubal Sterilization – Laparoscopy

Based on data from the CREST study involving over 9,000 women who underwent tubal sterilization by laparoscopy, major complications occurred at a rate of 1.6%, with unintended laparotomy as the most frequent complication²¹. Laparotomies were performed for the following reasons: unexpected bleeding, hematoma formation, viscous perforation (stomach and bowel), and fallopian tube resection. Rehospitalization occurred for the following reasons: pelvic infections, heavy vaginal bleeding, abdominal/pelvic pain, urinary tract infection,

¹⁹ Dominik R. Two Randomized Controlled Trials Comparing the Hulka and Filshie Clips for Tubal Sterilization. *Contraception* 62 (2000) 169-175.

²⁰ Sokal D. Two Randomized Controlled Trials Comparing the Tubal Ring and Filshie Clip for Tubal Sterilization. *Fertility and Sterility*. Vol 74, No 3, September 2000.

²¹ Jamieson DJ. Complications of Interval Laparoscopic Tubal Sterilization: Findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol* 2000; 96:997-1002.

peritonitis caused by bowel burn, bowel obstruction, etc. In an early report based on the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, the median postoperative hospital stay increased from 0 nights for women with no complications to 2 nights for women who had at least 1 complication²². The occurrence of a complication also increased the median total convalescence from 4 days to 14 days. More than one third (36%) of women who developed a complication had a total convalescence longer than 21 days, compared to only 2% of women with no complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparoscopy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (0.8%), primary incision complications (7.9%), infections (0.08%), and "other" (2.5%). The total complication rate in this study, for the complications reported, was 11.2%. In a similar study comparing the Filshie Clip with the Tubal Ring via laparoscopy²⁰, the following complications were noted: surgical injuries (2.2%), primary incision complications (4.4%), infections (0.4%), and "other" (1.0%). The total complication rate in this study, for the complications reported, was 8%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional method.

Finally, a large prospective study involving over 24,000 women who underwent tubal ligation using one of 5 methods²³ was conducted. In this study, the rate of surgical difficulties, which included anesthesia and equipment problems, etc., ranged from 2.4% to 12.5% (5.1% overall). The rate of surgical complications, which included uterine perforation, bowel injury, artery/vein injury, bladder injury, ovarian injury, etc., ranged from 0.7% to 2.7% (1.7% overall). The rate of

²² Destefano F. Complications of Interval Laparoscopic Tubal Sterilization. *Obstet Gynecol* 61:153, 1983.

²³ Bhiwandiwalla PP. A Comparison of Different Laparoscopic Sterilization Occlusion Techniques in 24,439 Procedures. *Am J Obstet Gynecol* 144:319, 1982.

technical failures, which required a change to a different technique or abandoning the procedure, ranged from 0.6% to 1.0% (0.8% overall).

Risks of Tubal Sterilization – Local vs. General Anesthesia

Based on early reports of the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, a fivefold difference in complication rates was found between procedures performed under general anesthesia and those performed under local anesthesia²². In subsequent reports from the CREST study involving over 9,000 women, use of general anesthesia was found to be a predictor of complications in women undergoing interval laparoscopic tubal sterilization²¹. In addition, 40% of the deaths attributable to tubal sterilization followed complications associated with general anesthesia, and there were no deaths due to complications from local anesthesia²⁴.

In a randomized, controlled trial comparing tubal ligation performed under local anesthesia to general anesthesia in 125 women, total procedure/post-surgery time was significantly shorter in the local anesthesia group¹⁴. In addition, the general anesthesia group had significantly more abdominal pain during the hospital stay, and use of analgesics immediately after surgery was more extensive. Also, the “awakeness” score was higher in the local anesthesia group the same evening as the procedure. Similar to these findings, in another randomized study comparing laparoscopic tubal ligation performed under local vs. general anesthesia²⁵, women in the local anesthesia group had a slightly shorter anesthesia time and recovery room stay. In addition, women in the general anesthesia group were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate of 110 or higher.

²⁴ Peterson HB. Deaths Attributable to Tubal Sterilization in the United States, 1977 to 1981. *Am J Obstet Gynecol* 146:131, 1983.

²⁵ Peterson HB. Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study. *Obstet Gynecol* 70:903, 1987.

Although use of local anesthesia for tubal sterilization is associated with a lower rate of complications, laparoscopic tubal sterilization still requires access to the peritoneal cavity with its associated risks.

Tubal Sterilization Risks – Pain/Return to Normal Activities

Finally, in a study of over 50 women using validated measures to assess the incidence, intensity and duration of pain following tubal ligation performed laparoscopically, it was found that 85% of women reported that pain and/or fatigue impacted their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of the procedure. The most powerful predictor of return to normal activity was the total amount of pain experienced. A separate study of 50 women undergoing laparoscopic tubal sterilization similarly found that the average number of days to resume normal activities was 4-6¹⁶. Also, as stated above, when tubal sterilization is performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

A New Contraceptive Alternative – The Essure System

Given the high unintended pregnancy, abortion and discontinuation rates associated with temporary methods of birth control, and the significant complications that can occur with the invasive surgery currently required for permanent birth control, we believe that women would benefit from a new contraceptive alternative that offers a less invasive method to achieve permanent birth control. As evidence of patient interest in such an alternative, is the statement made by a patient advocacy group to the FDA's OB/GYN Advisory Committee (panel). In February of 1996, Ms. Cindy Pearson, Program Director of the National Women's Health Network addressed the panel, which was convened to review the PMA for the Filshie Clip, stating: “. . . So we just wanted

to communicate a general sense that women are interested in alternative methods of sterilization. In particular, women are interested in methods that offer a safety or convenience advantage over the methods that are currently available to them.”.

The Essure System offers transcervical placement of the Essure Micro-insert, which can be accomplished without incisions or general anesthesia, with no loss of method effectiveness as compared to incisional tubal sterilization. Since the data that follow in this report demonstrate that this can be done safely and effectively to provide permanent birth control, we believe that this alternative will be embraced by women and their physicians, and will offer a significant public health benefit as a result.

Summary

In summary, due to the following points, we believe that there is strong evidence of the need for a new contraceptive alternative for women, especially a permanent method that can be performed without incisions or general anesthesia:

- An estimated half (48%) of pregnancies that occur in the United States each year are unintended, translating to an estimated 3,000,000 unplanned pregnancies in the United States each year.
 - The age group that has the second highest rate of unintended pregnancy is women aged 40-44.
- An estimated half of all unintended pregnancies result in abortion, translating to an estimated 1,000,000 abortions each year in the United States.
 - 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women over 30 years old.
- The morbidity associated with pregnancy is not infrequent or insignificant to the women or to society.

- There has been a documented risk to infants and children due to unintended pregnancies.
- Deaths and major complications occur with currently available methods of tubal sterilization due to general anesthesia and invasion of the peritoneal cavity that is associated with current methods.

We believe that many of the unintended pregnancies and abortions each year could be avoided if women had a permanent birth control option with an alternative risk/benefit profile than current methods.

Executive Summary of Clinical Data

Detailed data on the Pivotal Trial conducted to establish a reasonable assurance of safety and effectiveness for the Essure System are provided in the following sections. This section provides an Executive Summary of the data.

Protocol

Women in this study were followed at the following time points:

- One week-post device placement (PDP)
- 3-months PDP
- 3, 6, and 12 months post-alternate contraception (PAC)

In addition, women will be followed at 18 months PAC and annually for five years under post-market surveillance.

This figure provides an overview of the clinical trial visits.



Placement Rates

Of the 507 women in the Device Evaluation Group, bilateral placement was achieved in 464 (92%), and single Micro-insert placement was achieved in the 2 women with a unicornuate uterus (100%). Of the 41 women (8%) with bilateral tubes who did not achieve bilateral placement, 15 (37%) were found to have proximal tubal occlusion (PTO) on follow-up HSG. Eliminating these women from the analysis of placement rates results in an overall bilateral placement rate of 464/492 (94%).

Satisfactory Micro-Insert Location/Occlusion Rates

A total of 456/464 women (98%) with bilateral placement completed the 3-month post-device placement visit and underwent an HSG. Of those 456 women, 437 (96%) were noted on HSG to have Micro-inserts in satisfactory location. Of those

437 women, 421 (96%) were also noted to have bilateral tubal occlusion. Nine of the 19 women with Micro-inserts in unsatisfactory location returned for a second placement procedure to replace an expelled Micro-insert. All achieved bilateral placement and were found on follow-up HSG to have bilateral occlusion and Micro-inserts in satisfactory location. All of the 16 women who had tubal patency at the initial HSG chose to undergo a second HSG 3 months later, and all were found to have bilateral occlusion on the second HSG. Therefore, of the 456 women with bilateral placement completing the 3-month visit, 446 (98%) were ultimately found to have Micro-inserts in satisfactory location and bilateral occlusion. In addition, 100% (446/446) of the women with Micro-inserts in satisfactory location ultimately had bilateral occlusion.

Reliance Rates

As stated above, 446/456 women (98%) with bilateral placement completing the 3-month PDP visit were able to rely on Essure for contraception. In addition, 3 women with bilateral placement did not have an HSG but chose to begin relying on Essure. Also, four women with unilateral placement and either confirmed contralateral PTO (2) or a unicornuate uterus (2) were able to rely on Essure for contraception. Therefore, among the 507 women in the Device Evaluation Group, 453 (89%) were ultimately able to rely on Essure for contraception, and among the women with bilateral placement, 449/464 (97%) were ultimately able to rely on Essure for contraception. These percentages are conservative since they count lost-to-follow-up women as “not relying”.

Adverse Event Rate

Adverse events on the day of the placement procedure were reported in 17 (3%) women. All events were resolved prior to the woman being discharged from the recovery room, except for one woman who required overnight observation following an adverse reaction to pain medication. Day of procedure adverse

events included the following, all of which occurred in <1% of cases: vomiting, vaso-vagal response, hypervolemia, band detachment, perforation, excessive vaginal bleeding, and “other” (skin itching, bloating, loss of appetite, and reaction to saline used for uterine cavity distension).

Adverse events that *initially* prevented the woman from relying on Essure occurred in 21 (4.5%) women. These were primarily Micro-insert expulsions following original Micro-insert placement that was out-of-specification. Nine of the women who experienced an expulsion chose to undergo a second placement procedure, and all were successful. Therefore, including the perforation that was diagnosed on the day of placement, adverse events that *ultimately* prevented reliance occurred in only 12 women (2.6%). The most frequently reported adverse events reported in the first year (fifteen months PDP) that did not prevent the woman from relying on Essure, but were rated by the Investigator as at least “possibly” related to Essure, were back pain (8.4%), and abdominal pain/cramps (3.4%). All other events occurred in less than 3% of women.

Patient Satisfaction/Comfort

Women in the study consistently rated their overall satisfaction and comfort in wearing the Micro-inserts as very high. One-week post-device placement, >95% of women rated their comfort as “good” to “excellent” and their satisfaction as “somewhat satisfied” to “very satisfied”. At all subsequent study visits, 99% of women rated their comfort with wearing Essure as “good” to “excellent”. At all study visits, at least 98% of women rated their overall satisfaction as somewhat to very satisfied (this included women who were not able to rely on Essure).

Pregnancy Prevention

There have been no pregnancies in any of the 453 women who have relied on Essure for contraception (449 with bilateral placement). There are 408 women

with bilateral placement who have been followed for at least one-year after relying on Essure for contraception and 14 women who began relying on Essure but subsequently were lost-to-follow-up (there are 3 additional women who were lost-to-follow-up prior to the 3-month PDP visit, at which women are told whether they can begin relying on Essure). The remaining 27 women with bilateral placement who are relying on Essure have completed from 7-11 months of follow-up.

There were 4 luteal phase pregnancies reported in the Pivotal trial (pregnancies occurring prior to Essure Micro-insert placement but not detected on the day of placement). None of these 4 women became pregnant while relying on Essure for contraception. Each of the pregnancies in these four women was terminated, and each of the four women was subsequently able to rely on Essure for contraception and has not reported a pregnancy while relying on Essure.

Combined with data from the Phase II study of Essure, this equates with over 627 women-years of first year effectiveness evaluation (and 272 woman-years of second year evaluation).²⁶ The current estimate of the one-year effectiveness rate based on these combined data is 99.84%.

Summary

In summary, we believe that the data contained in this Pivotal Trial Report, together with the data provided elsewhere in the PMA, provide a reasonable assurance of the safety and effectiveness of the Essure System based on valid scientific evidence.

²⁶ One woman in the Phase II trial who received a prior device design (Beta Design of the STOP Device) that was discontinued in 1998 became pregnant after relying on the discontinued design for 2 years. This pregnancy is not included in the Phase II effectiveness calculation since it is a different device than that for which approval is being sought. The device studied in the Pivotal trial is the Gamma version of the STOP device. The Gamma version has been trademarked as "Essure". All prior versions are referred to as "STOP" with a version name: alpha or beta.

B. Background

Four separate studies of the Essure System were conducted as part of the clinical development of the product. Each is depicted in the graphic below.

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The reports of the first 3 studies were included in PMA Module I, Module III and Module V, respectively. Unlike prior clinical trials, the Pivotal Trial included evaluation of the gamma design only.

The IDE for the Pivotal Trial of the Essure System (G000055) was submitted to the FDA on February 28, 2000, following a pre-IDE meeting on November 19, 1999. Conditional IDE approval was received on March 24, 2000, and final IDE approval was received on September 7, 2000.

It should be noted that this report reflects the study protocol and statistical plan that were approved under the IDE. Approximately 10 months after final IDE approval, on June 29, 2001, a Determination/Agreement meeting was held with the Agency to make binding the agreements reached during the IDE approval process. Binding agreement was reached for the majority of the earlier agreements under the IDE. The two exceptions were: 1) filing the PMA if only a 95% effectiveness rate was established, and 2) use of the CREST study as a historical control. Agreement to use the CREST study as a “qualitative benchmark” as opposed to a statistical control group was reached, however.

Because this Report necessarily reports on the approved protocol and statistical plan, it makes reference to use of the CREST study as a historical control and the original 95% effectiveness rate. The 95% effectiveness rate target is now a moot point, as the data support a one-year effectiveness rate that is substantially higher; however, the statistical plan attached is the one approved under the IDE, so it still references the 95% effectiveness rate target.

We provide this background to let the Agency know that we acknowledge the lack of binding agreement on the above two items, and to clarify that this Report necessarily contains and reflects the original IDE approved documents (protocol, statistical plan), since there are no other approved documents to report against.

C. Study Design/Endpoints

The Pivotal Trial of the Essure System (formerly known as STOP) was designed as a multi-center, non-randomized, single-arm, international study of women seeking permanent contraception. The study was conducted in the U.S., Europe, and Australia. The targeted study population was 400 women in whom bilateral Micro-insert placement was achieved. It was expected that more than 400 women would need to be enrolled in order to obtain 400 women in whom bilateral placement was achieved.

The primary endpoints for this study were:

- Prevention of pregnancy;
- Safety of the Micro-insert placement procedure; and
- Safety of the Micro-insert wearing.

The secondary endpoints for this study were as follows:

- Participant satisfaction with the Micro-insert placement procedure;
- Participant satisfaction with Micro-insert wearing;
- Bilateral Micro-insert placement rate; and
- Development of a profile for an appropriate candidate for the Essure procedure.

The study was designed to include 5 years of post-alternative contraception follow-up, 1 year of which was to be completed prior to a PMA filing. The remaining 4 years will be completed as part of post-market surveillance. Binding agreement to file the PMA based on one-year follow-up of 400 women has been reached (see letter from FDA dated August 2, 2001, **Exhibit A**). Subsequent to the binding agreement, FDA accepted our proposal to file the PMA with one-year follow-up visits completed on 350 women (see FDA letter dated March 15, 2002, **Exhibit A**).

It should be noted that the study had two phases: 1) the “Post-Device (Micro-insert) placement” (PDP) phase, and 2) the “Post-Alternative Contraception” (PAC) phase. The “Post-Device Placement” phase was the time period between Micro-insert placement and the 3-month visit, during which women were instructed to rely on alternative contraception. At the 3-month visit, a hysterosalpingogram (HSG) was conducted to evaluate Micro-insert location and tubal occlusion. Assuming both were satisfactory, women were instructed to discontinue alternative contraception, thus entering the “Post-Alternative Contraception” (PAC) phase of the study, during which they relied on Essure solely for contraception. If the HSG was not satisfactory, then, depending on the circumstances, women were instructed to either seek alternative contraception or remain in the “Post-Device Placement” (PDP) phase until a second HSG or Micro-insert placement procedure was performed.

D. Clinical Trial Conduct/GCP Compliance Statement

The study was conducted in compliance with Good Clinical Practices (GCPs) – 21 CFR, Parts 50, 54, 56 and 812. All sites conducted the study according to the same protocol as that approved by the FDA (IDE # G000055) and by the Medical Device Authority (MDA) in the United Kingdom. All sites also obtained approval from an Institutional Review Board (IRB)/Ethics Committee (EC) before study commencement.

(b) (4)



E. Clinical Trial Monitoring

(b) (4)



(b) (4)



F. Study Population/Selection Criteria (Inclusion/Exclusion)

Study candidates were women seeking permanent contraception. Permanent contraception candidates were screened for eligibility to participate in this clinical study. Candidates who met the inclusion and exclusion criteria and who were willing to participate in the study were provided with an Informed Consent form for their review and signature prior to screening tests.

The objectives of the inclusion and exclusion criteria were to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

The detailed inclusion and exclusion criteria are provided in the protocol, **Volume 3 of the April 19, 2002 PMA, Exhibit A.**

G. Control Population

(b) (4)



²⁷ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996; 174:1161-70.

²⁸ See Appendix A to February 3, 2000 submission in follow-up to Pre-IDE meeting, as well as Section X of the original IDE application, and Appendix E of August 7, 2000 response to 2nd conditional approval letter.

H. Investigational Sites

(b) (4)



I. Number of Investigators/Number of Subjects per Investigator

(b) (4)



Table 1. Investigators/# Women Scheduled for Micro-insert Placement Procedure

Location	Investigator	Site number	No. Women
(b) (4), (b) (6)			

J. Clinical Protocol

The complete protocol is provided in **Volume 3 of the April 19, 2002 PMA, Exhibit A**. The Informed Consent form for the study is provided in **Volume 3 of the April 19, 2002 PMA, Exhibit B**. The Patient Questionnaires and the electronic Case Report Forms for the study are provided in **Volume 4 of the April 19, 2002 PMA²⁹**. A flowchart of the study sequence can be found below in **Figure 1**, followed by a brief summary of each protocol visit.

(b) (4)



Eligibility

The eligibility phase, through screening questions, counseling, and physical exam and labs, was designed to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

Screening

(b) (4)



Micro-insert Placement

Day of procedure activities were to:

- Conduct a pregnancy test, pre-procedure
- Review counseling, pre-procedure
- Perform the Micro-insert placement procedure
- Conduct the pain assessment and satisfaction questions post-procedure
- Conduct the X-ray verification of Micro-insert placement
- Provide post-procedure instructions, covering patient diaries/questionnaires and need for alternative contraception until 3-month PDP visit

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K. Study Period

(b) (4)



³⁰ Some women had second device placement procedures that occurred beyond this date. All such procedures occurred by June 2001.

L. Investigational Device Accountability

The Investigational device accountability information is provided in **Exhibit B**.
There was complete accountability for all study devices.

M

M. Statistical Methods

(b) (4)



N

N. Patient Tree

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(b) (4)



(b) (4)



O. Withdrawn/"Safety Only" Women

(b)(4)(b)(6)- Patient Enrollment Data



(b) (4)



P. Patient Demographics

(b)(4)(b)(6)- Patient Enrollment Data



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(b) (4)



Q. Study Deviations

(b) (4)



R. Study Results

(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



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³⁵ See second conditional approval letter dated June 21, 2000, item #34.

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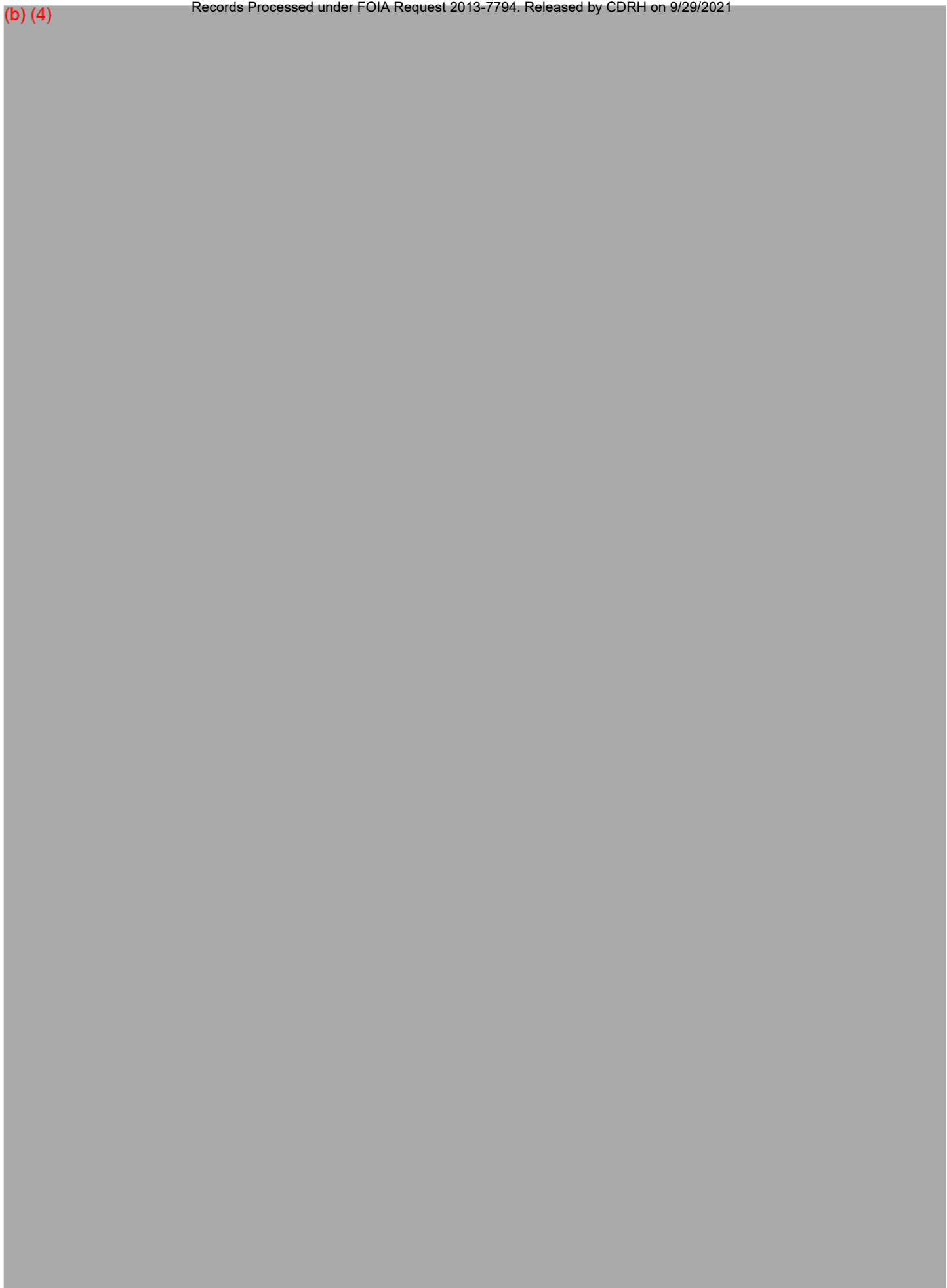
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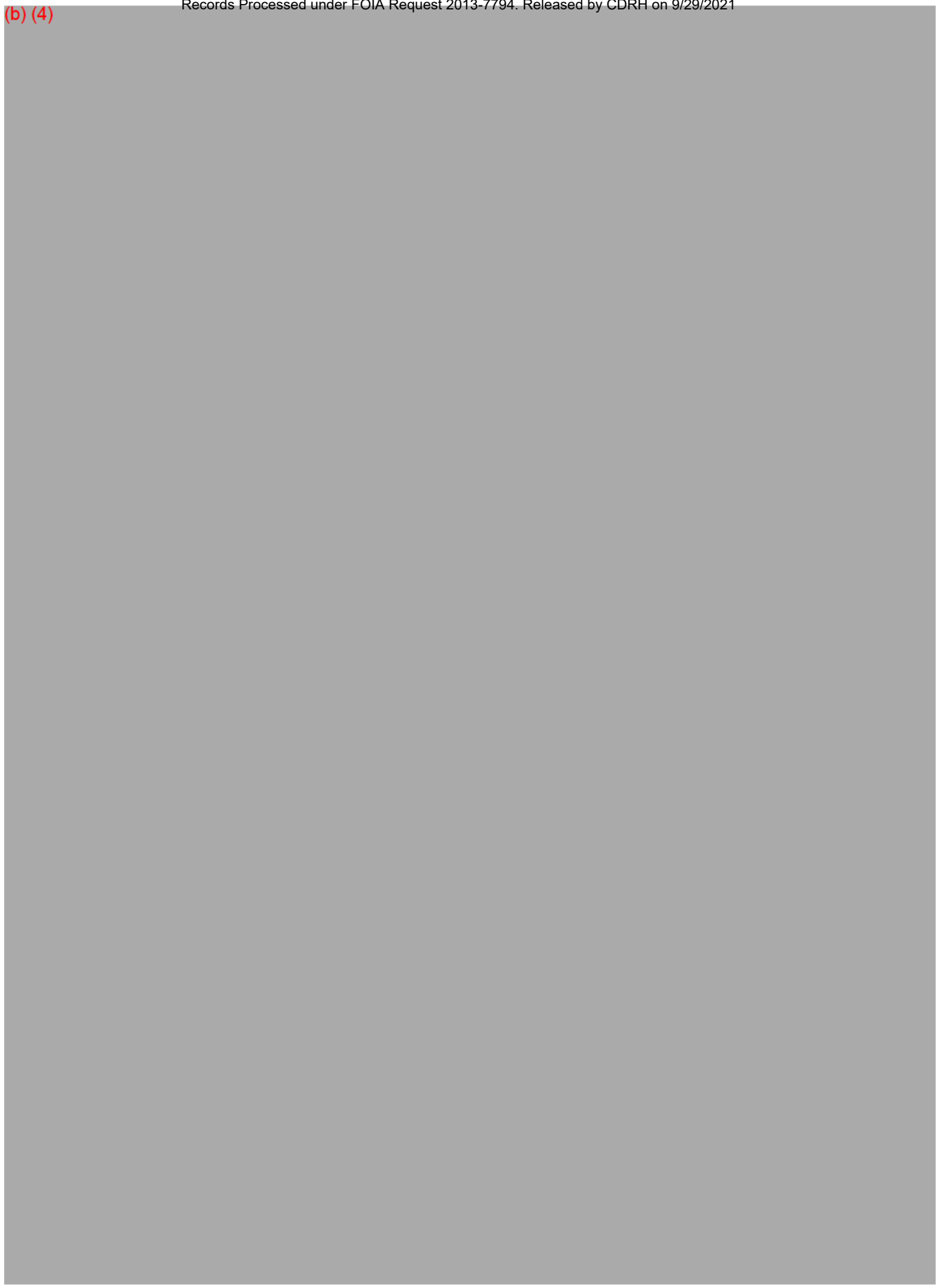
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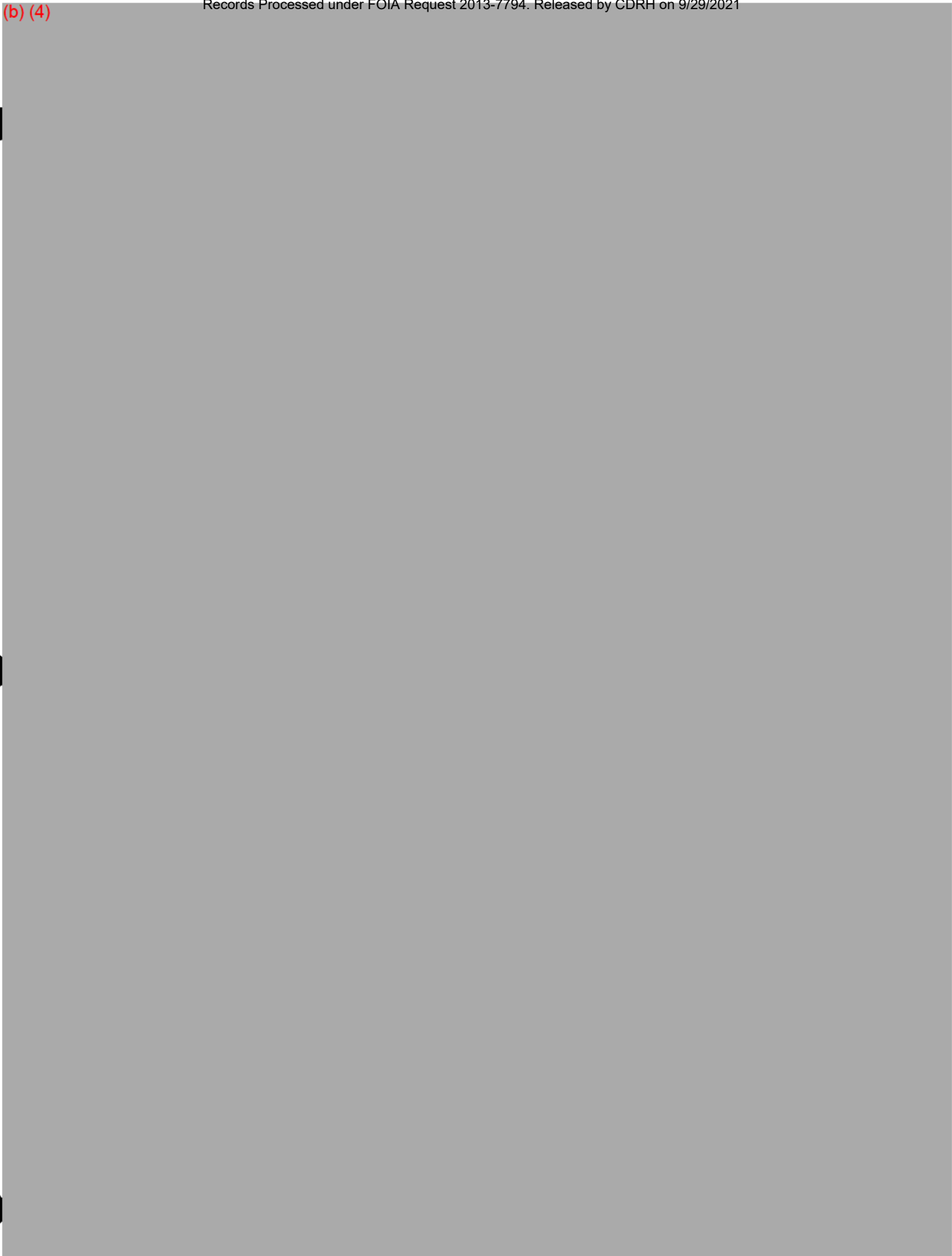
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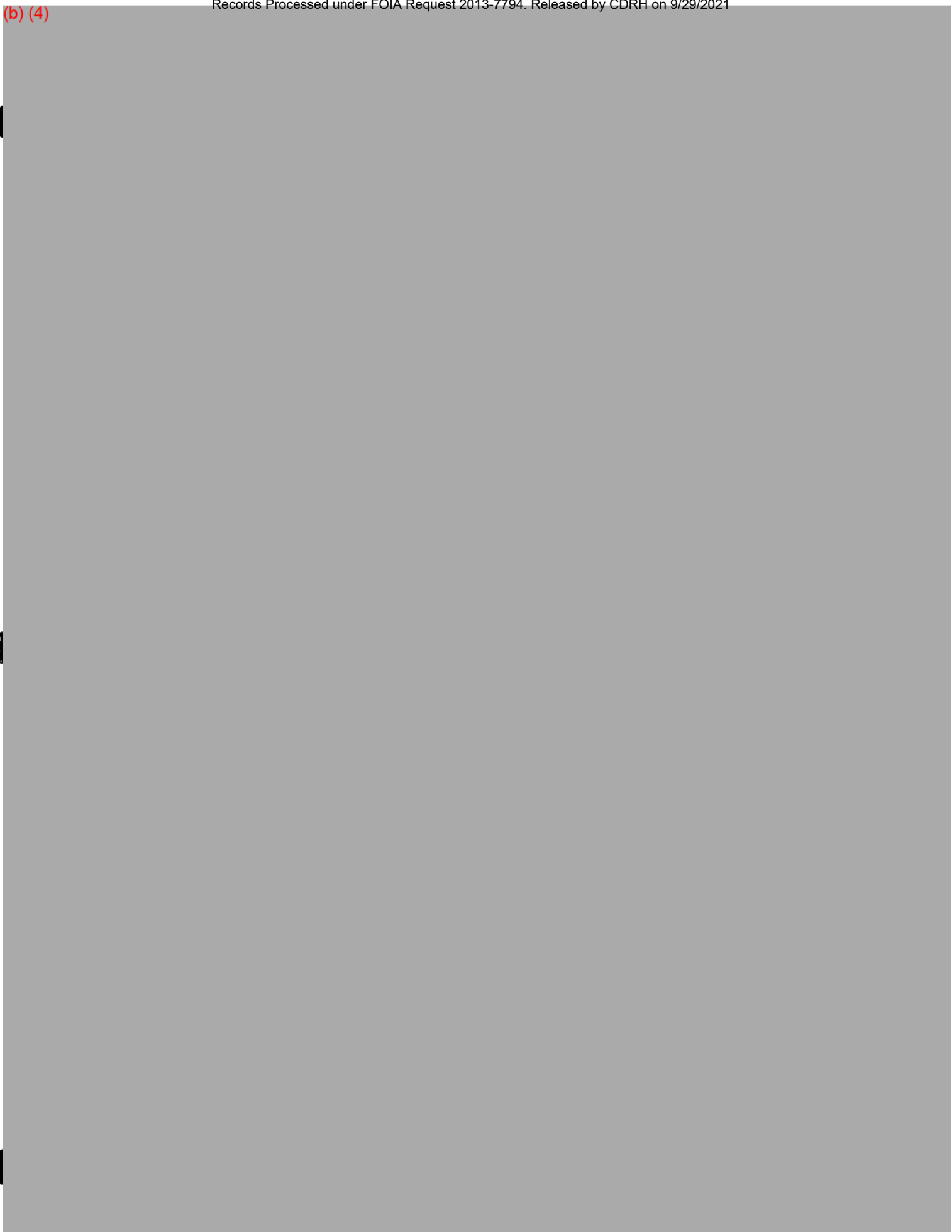
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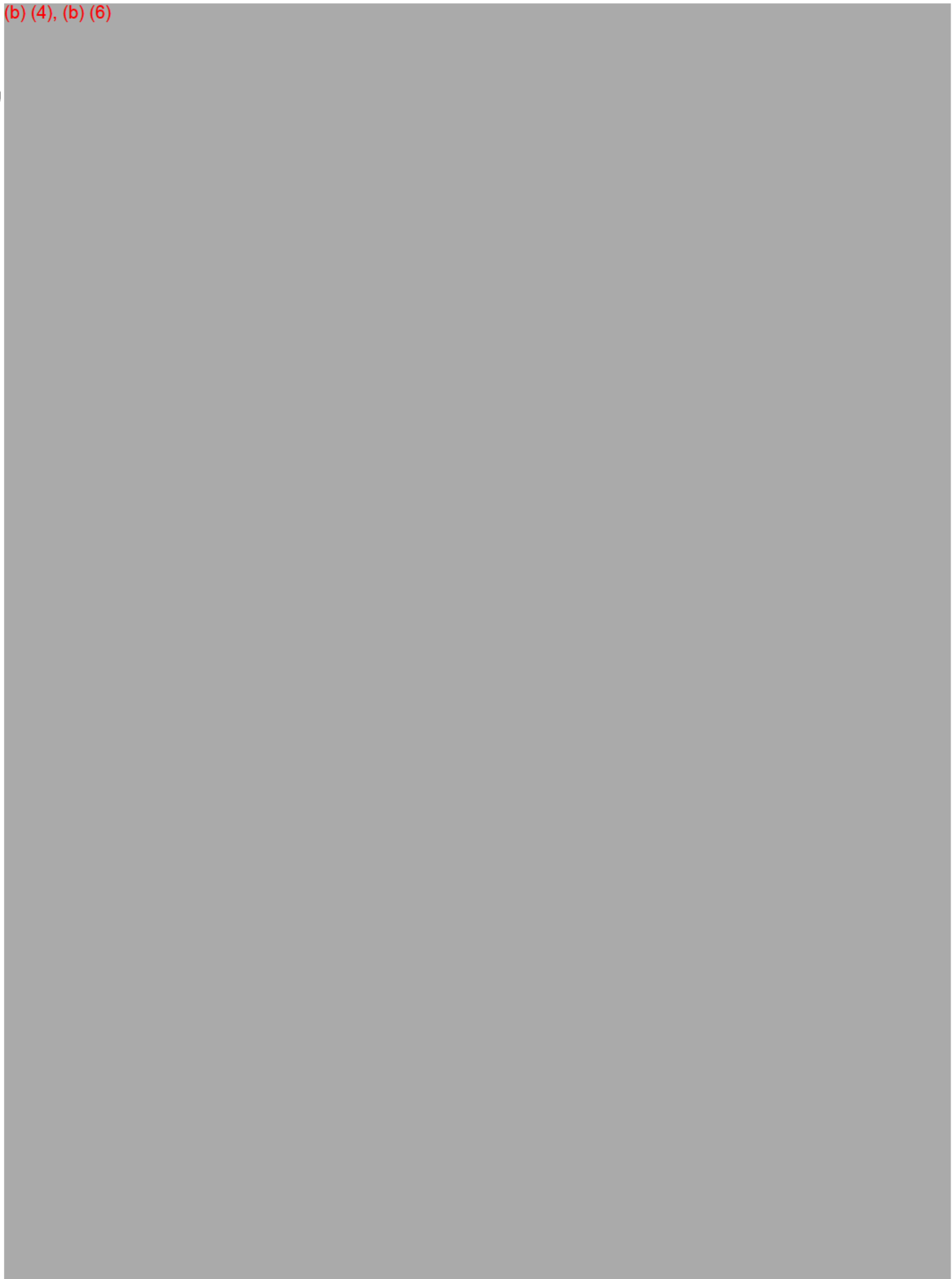
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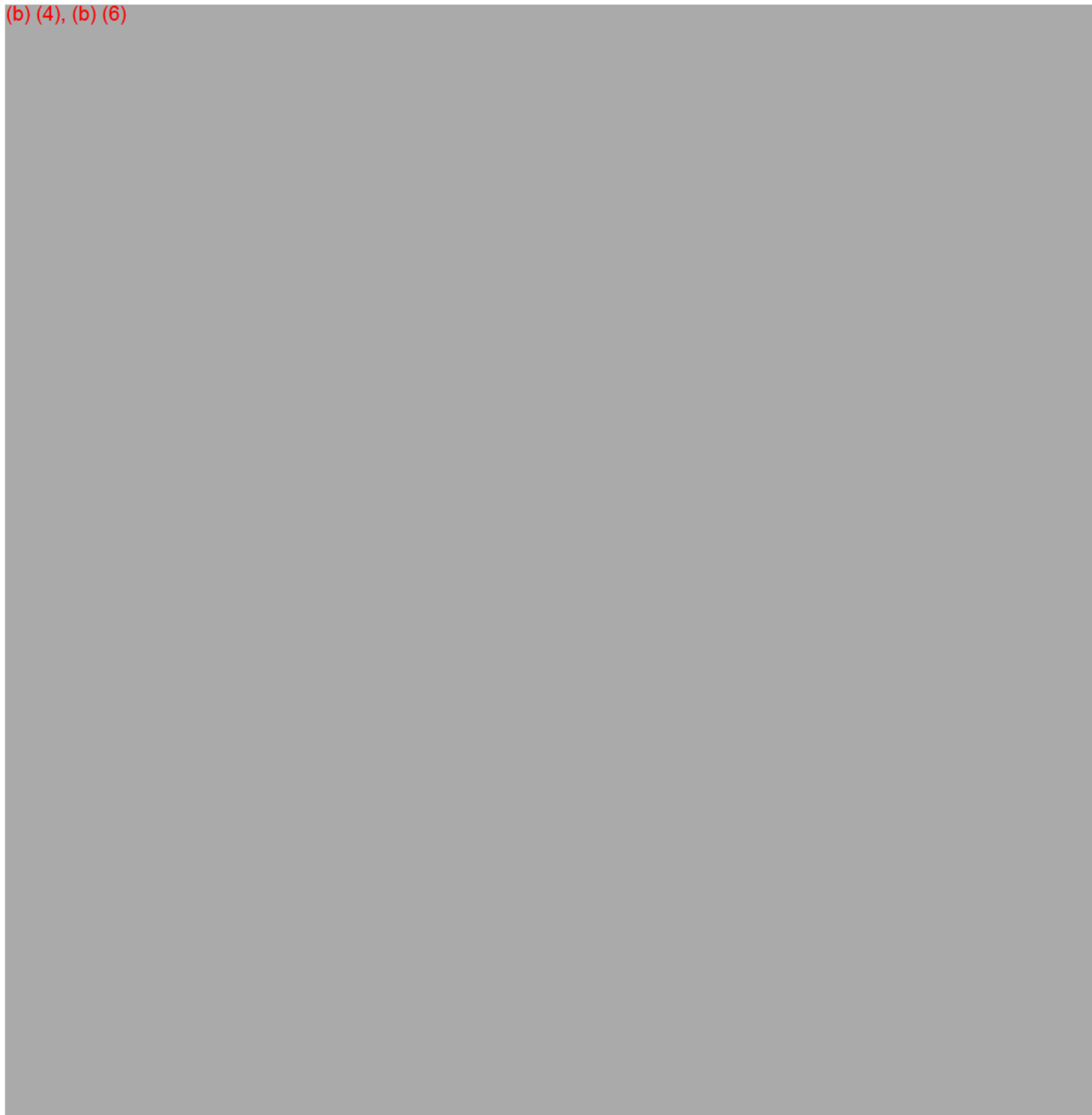
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⁴⁶ Fraser I. S. et. al. A preliminary study of factors influencing perception of menstrual blood loss volume. Am J Obstet Gynecol 788-793, 1984.

⁴⁷ Wilcox, L. et. al. Menstrual Function after Tubal Sterilization. Am J Epidemiology Vol. 135; No. 12 1368-1381. 1992.

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Table 45. Adverse Events Preventing Reliance Among Bilateral Placements

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7. **Effectiveness**

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Censoring

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S. Justification for Use of Foreign Data

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T. Conclusions Drawn from the Study

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U. Risk to Benefit Analysis

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V. Case Report Forms for Lost to Follow-up Participants

Case Report Forms for lost-to-follow-up women are included in **Volumes 5-7**.

W. Summary Data Tables

Summary data tables for the data freeze as of May 24, 2002 are included in **Volumes 8-10.**

Exhibit A - FDA Correspondence
Binding Agreement (FDA Letter August 2, 2001)
Early PMA Acceptance (FDA Letter March 15, 2002)

PMA Amendment

Report of Pivotal Trial: June 5, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

**Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850**

MAR 15 2002

(b) (6)



RECEIVED
MAR 15 2002
BY: _____

Conceptus, Inc.
1021 Howard Avenue
SAN CARLOS CA 94070

Re: M010031 Early Submission of PMA Application for Essure System
Received: December 21, 2001
Amended: February 13, 2002

Dear (b) (6) :

(b) (4)



(b) (4)

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If you have any questions, please call (b) (6)

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Sincerely yours,

(b) (6)

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Center for Devices and Radiological Health



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

RECEIVED
AUG 10 2001
BY: _____

AUG 2 2001

(b) (6)

Conceptus, Inc.
1021 Howard Avenue
San Carlos, California 94070

Re: I010178 – 513(a)(3)(D) Determination and 520(g)(7) Agreement Meeting
STOP™ System (Selective Tubal Occlusion Procedure) Device
Received: May 22, 2001
Amended: July 17, 2001

Dear (b) (6) :

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Page 2 – (b) (6)

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Page 3 - (b) (6)

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The agreement decision is binding on the Center for Devices and Radiological Health. It can be changed only with the written agreement of the sponsor or when there is a substantial scientific issue essential to determining the safety or effectiveness of the device, and only following an opportunity for the sponsor to meet with CDRH to discuss the scientific issue involved. Details of our determination/agreement meeting are enclosed.

If you have any comments or questions regarding this letter, please contact

(b) (4), (b) (6)

Sincerely yours,

(b) (6)

Center for Devices and
Radiological Health

Enclosure

Minutes of Meeting

Participants:

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Date: June 29, 2001

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Prepared (b) (6) – 7/12/01
Revised: 7/17/01, 7/20/01, 7/23/01, 7/26/01, 7/30/01

Exhibit B - Investigational Device Accountability

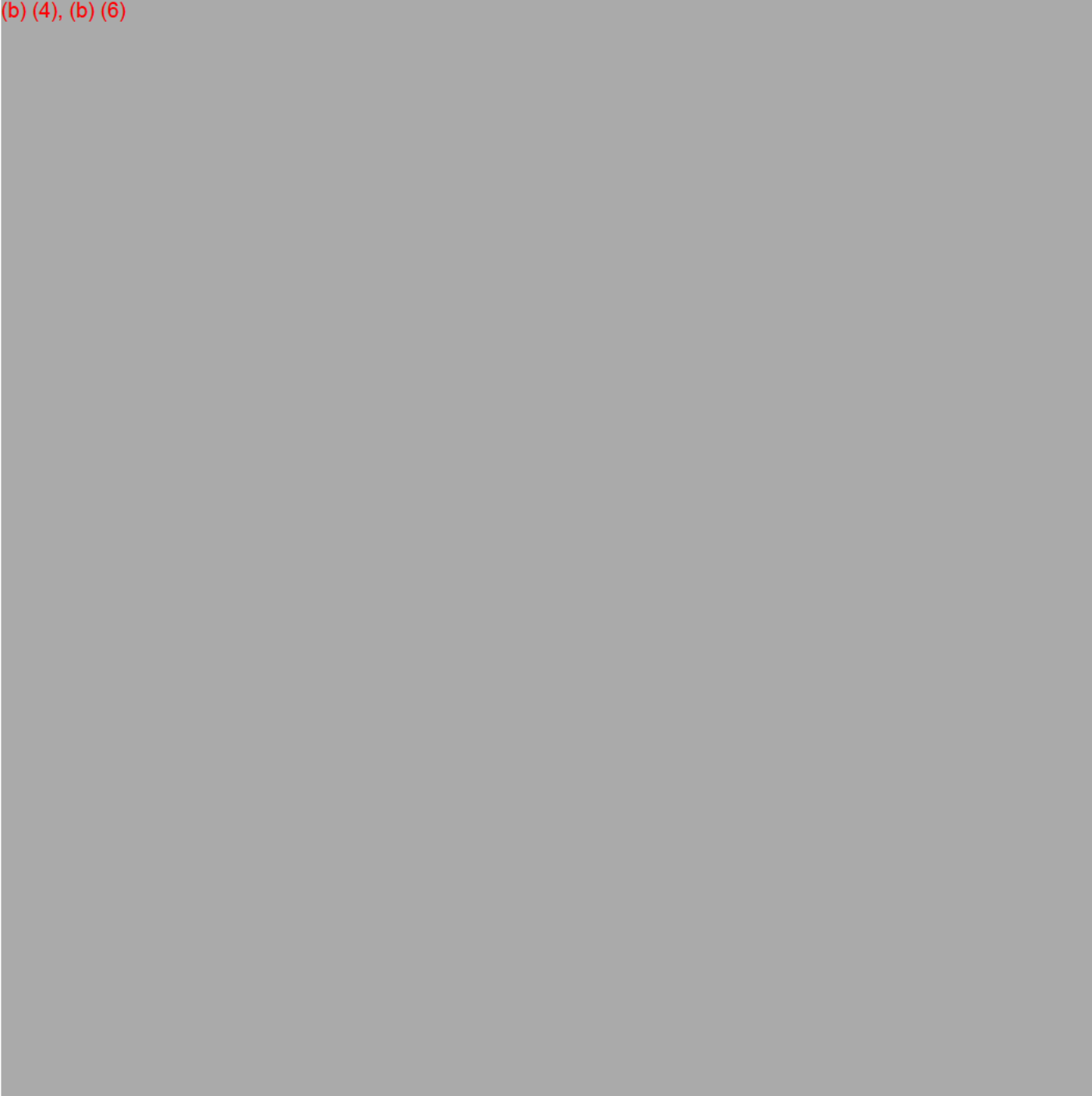
PMA Amendment

Report of Pivotal Trial: June 5, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

Exhibit B - Investigational Device Accountability

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⁵⁶ 5-day notification dated October 27, 2000; G000055/S8.

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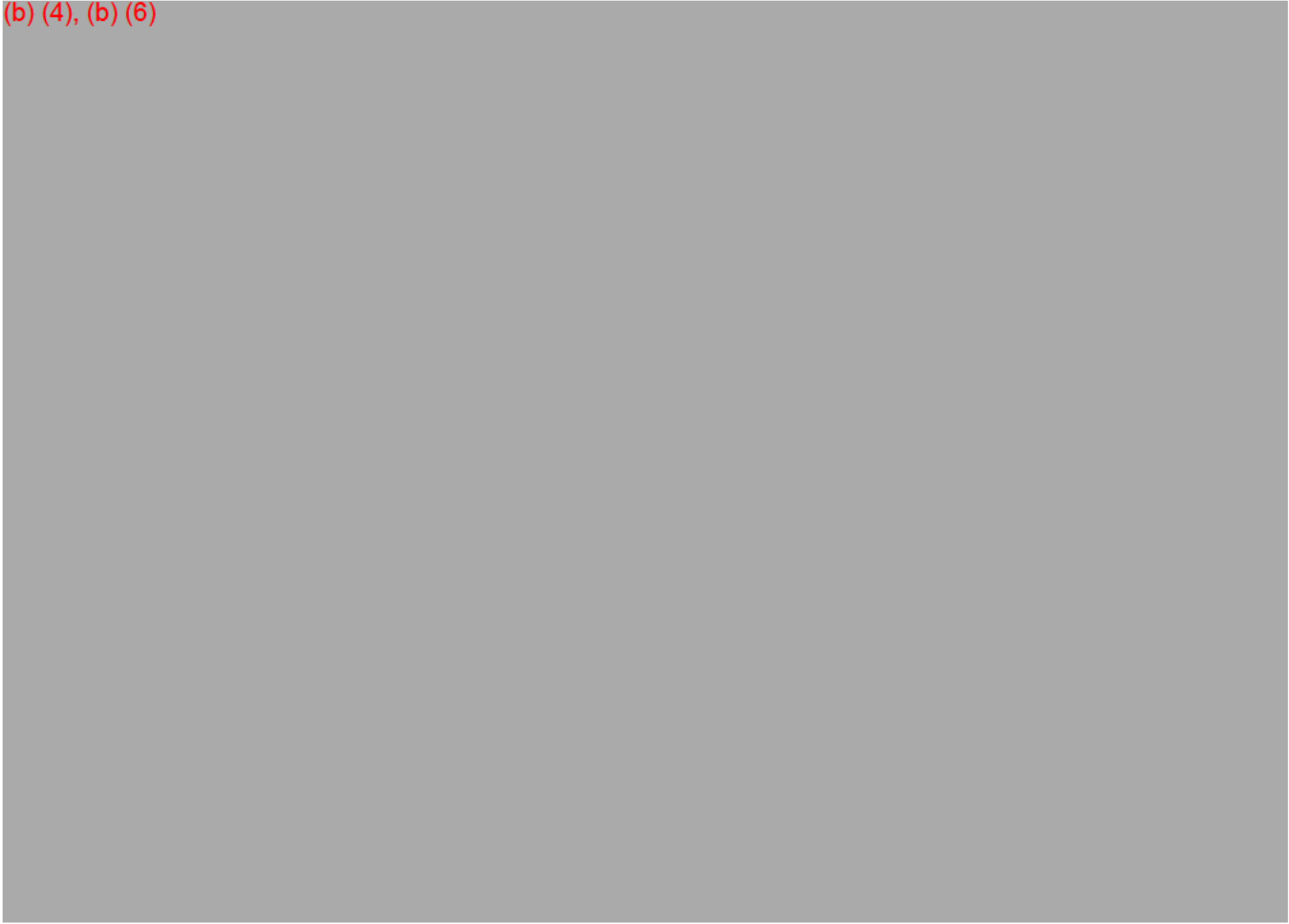


Exhibit C - Study Deviations

Exhibit C - Study Deviations

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Exhibit D - Luteal Phase Pregnancies

Exhibit D - Luteal Phase Pregnancies

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⁵⁷ Wilcox AJ, Baird DD, Dunson D, et. al. Natural limits of pregnancy testing in relation to the expected menstrual period. JAMA Vol 286 No. 14, Oct 10, 2001.

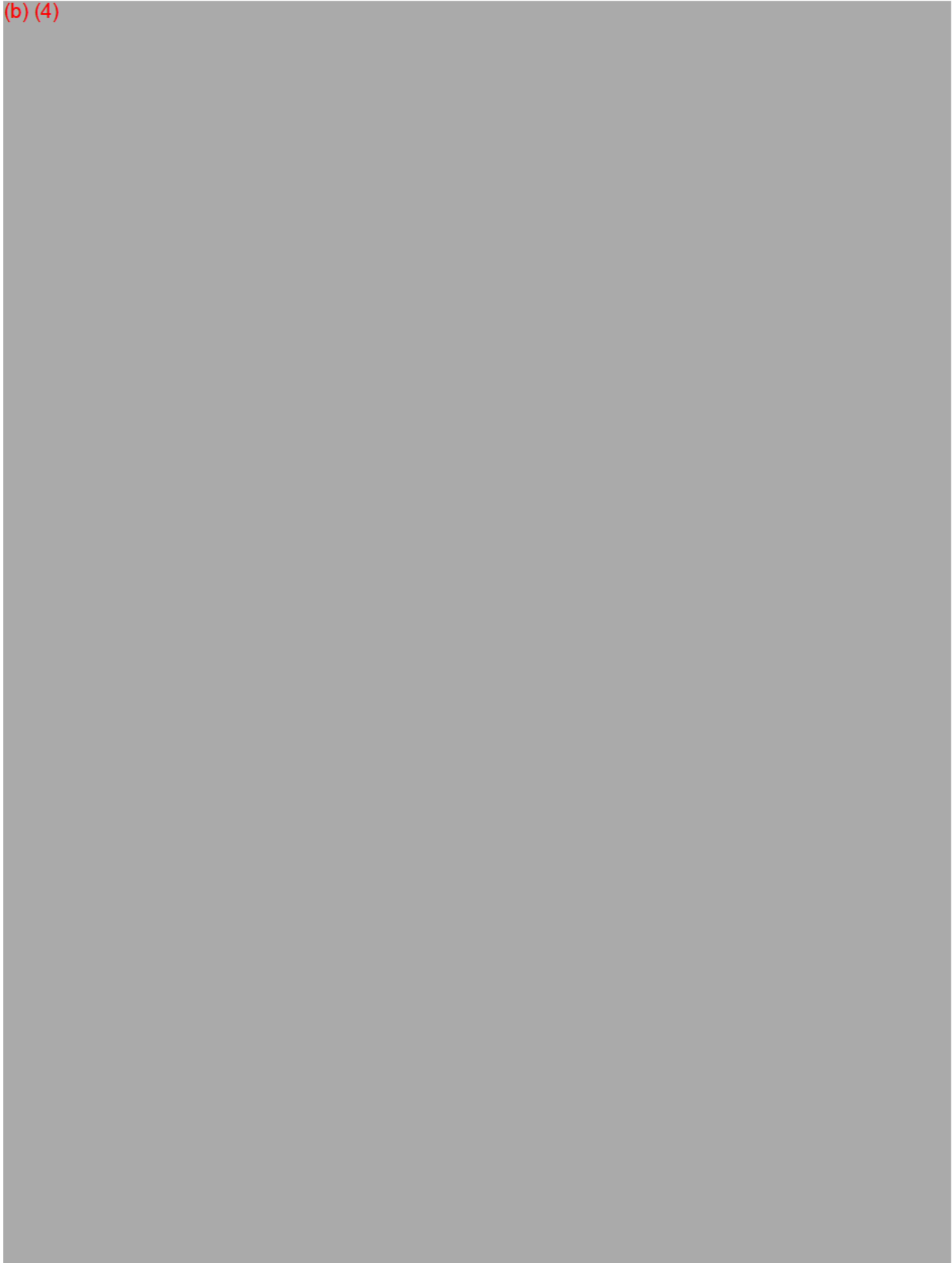
⁵⁸ Peterson HB, et.al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996; 174:1161-70.

⁵⁹ The CREST data was collected at a time when early pregnancy testing was not available. Thus, women who did not have an advancing pregnancy were likely never diagnosed if they had early pregnancy loss. Whereas in our study, women were diagnosed very early and in fact one pregnancy was also spontaneously resolving at the time of diagnosis.

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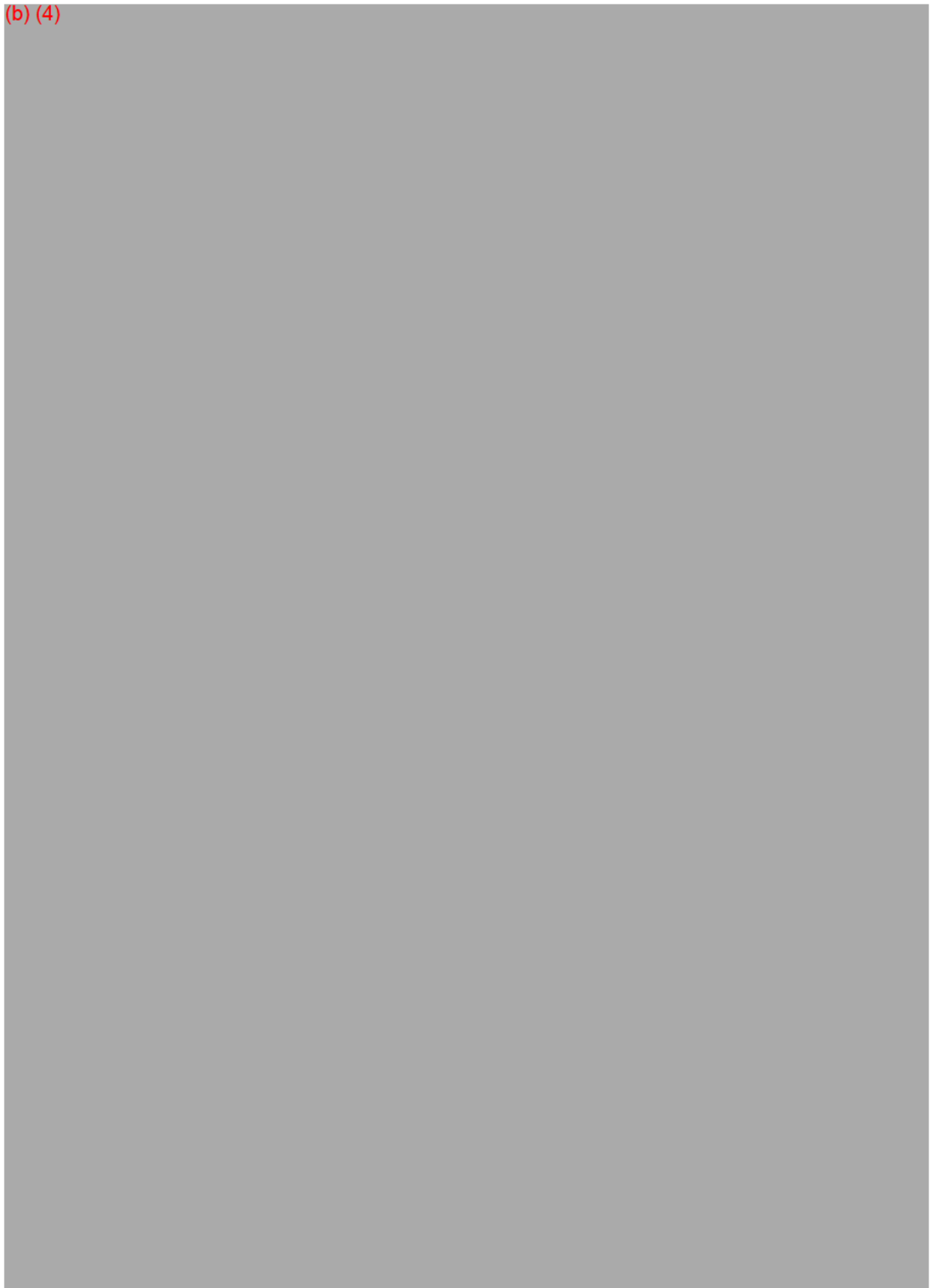
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Exhibit E - Predictors of Placement Failure

PMA Amendment

Report of Pivotal Trial: June 5, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

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⁶⁰ A woman could have had any of the above outcomes, so the number excluded in the analysis was not the sum of the figures presented.

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Table 2. Demographic variables and placement success

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Exhibit F

Exhibit F – Learning Curve Analysis

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Exhibit G: Draft Manuscript

**Exhibit H – Histology Picture from Perforated Micro-insert
(b) (6) removed from peritoneal cavity**

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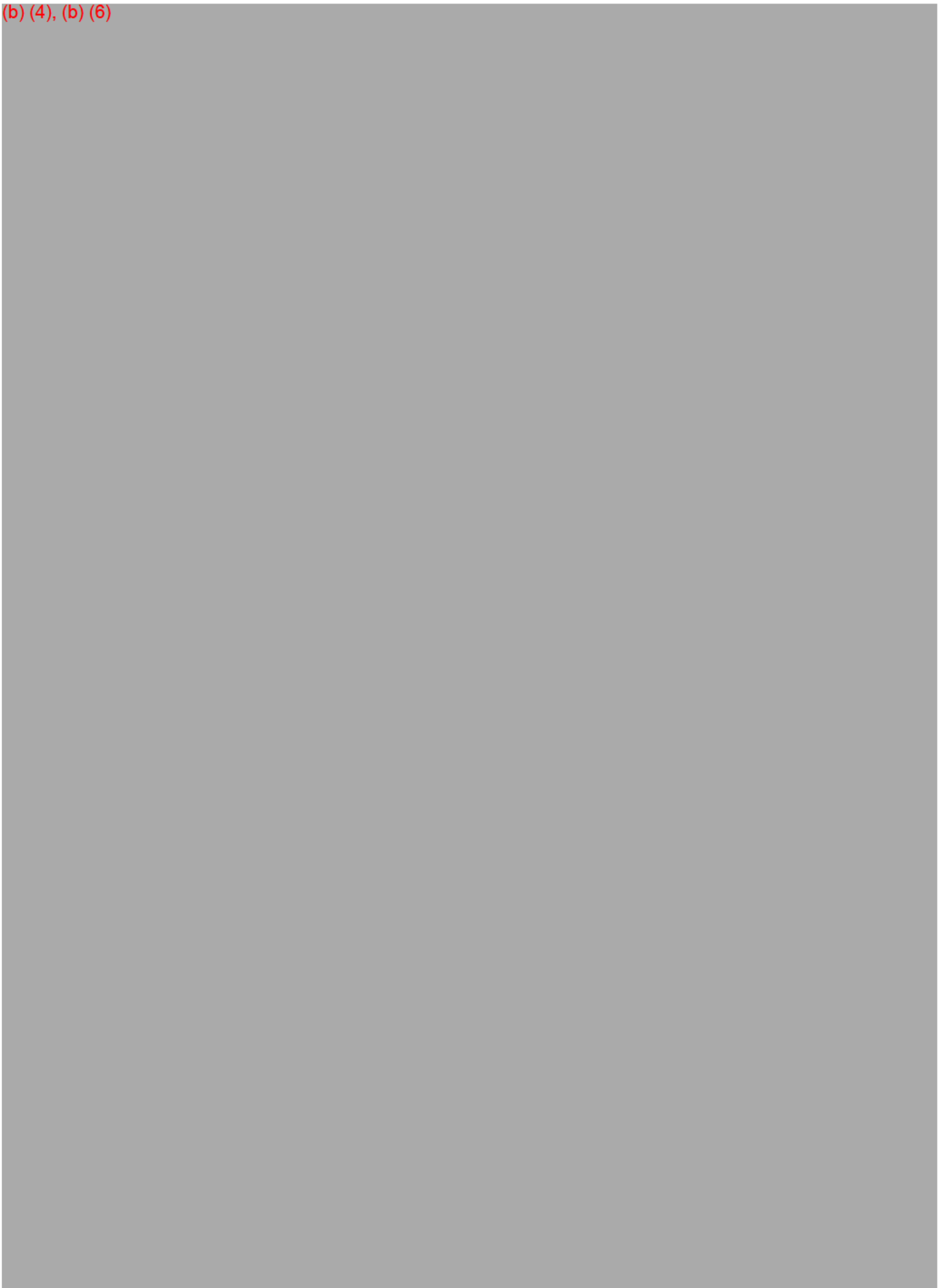


Exhibit I – Censoring Analysis for Effectiveness Calculation

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Exhibit J - Country-by-Country Analysis of Placement, Adverse Events Preventing Reliance and Reliance Rates

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Exhibit K-

Listings by Site of Adverse Events

Listing by Site of Protocol Deviations

Adverse events by site (Table number refers to Pivotal trial report table number)

Site	Investigator	Subject Number	Table Number	Adverse Event
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Deviations by site

Site	Investigator	Subject Number (all are S2000-)	Description of Deviation
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Conceptus Essure™ System

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AMENDMENT. PLEASE REFER TO VOLUME 3 OF APRIL 19, 2002
PMA FOR THE BELOW DOCUMENTS**

- Exhibit A** - Study Protocol
- Exhibit B** - Informed Consent Form
- Exhibit C** - Statistical Plan (Final Clean Copy)
- Exhibit D** - Statistical Plan (with Changes Noted)

001-1-2002

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Exhibit A - Patient Questionnaires

Exhibit B - Electronic Case Report Forms

JUN 5 2002

JUN - 7 2009

Conceptus Essure™ System

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- N. Patient Tree
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- Table 29 -** Is the Woman Employed?
- Table 30 -** Days of Work Missed (for those who are employed)
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- Figure 2 -** Patient Tree
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Volumes 5 –7

Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

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Volumes 8-10

Summary Data Tables:

- Number 1 - Patient Enrollment and Reasons for Discontinuation**
- Number 2 - Months of Wearing**
- Number 3 - Months of Effectiveness**
- Number 4 - Demographics and Baseline Characteristics**
- Number 5 - Device Placement Procedure**
- Number 6 - Anesthesia**
- Number 7 - Post-procedure Pain and Recovery**
- Number 8 - Adverse Event on Day of Placement**
- Number 9 - HSG Results for Unsuccessful Placement**
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- Number 20 - Investigator reliance by country**

Volume 11

References for Pivotal Trial Report

PMA
Conceptus, Inc.

Volume 12

Proposed Labeling (Product, Patient, Professional)

Professional Training Program

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Visit: Screening

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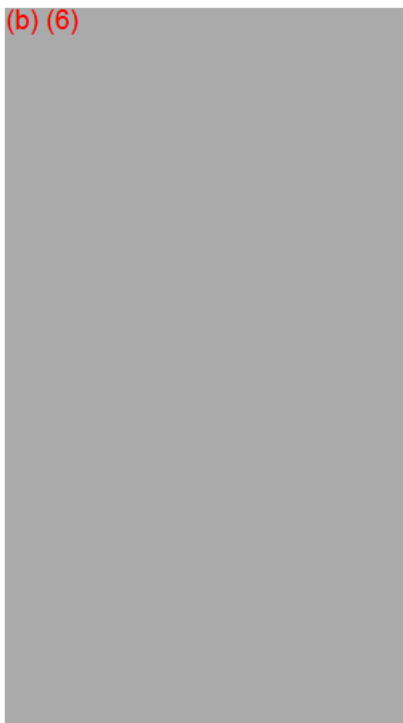
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Conceptus Essure™ System

Amendment to PMA No. P020014

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ACOG Technical Bulletin #222 – April 1996

Sterilization

Over 170 million couples worldwide use surgical **sterilization** as a safe and reliable method of contraception. In the United States, **sterilization** is the most commonly used method among married or formerly married women. An estimated 640,000 female **sterilization** procedures and 500,000 male **sterilization** procedures are performed each year (1, 2). In 1988, **sterilizations** accounted for 39% of contraceptive method use by all women 15-44 years old; 27.5% of women using contraception had undergone tubal **sterilization**, and 11.7% reported that their partners had undergone vasectomy (3).

Patient Counseling and Selection

Patients should be informed about both male and female **sterilization** as well as the risks and benefits of alternative long-acting, temporary contraceptive methods (see the box). When appropriate, the male partner can be included in such initial counseling. Many men and women have the impression that **sterilization** operations are easily reversible. The clinician should make clear to the patient that all operative **sterilizations** are intended to be permanent. Counseling should take into account risk factors that affect regret of **sterilization**. In the United States, the strongest indicator of future regret is young age at the time of **sterilization**, regardless of parity or marital status. Women between the ages of 20 and 24 years at **sterilization** are twice as likely to experience poststerilization regret as women **sterilized** between the ages of 30 and 34 years (4). Marital instability increases the probability of regret. Approximately 6% of **sterilized** women report regret or request information about **sterilization** reversal within 5 years of the procedure; urologists estimate that close to 1-2% of the total number of men they **sterilize** seek information on vasectomy reversal (4, 5). Although success rates in vas and tubal reanastomosis have improved dramatically in recent years, successful reversal and subsequent pregnancy depend on many factors, including the type of **sterilization**, interval between **sterilization** and reversal, age, and length of the remaining tube.

Preoperative counseling should include an explanation of the causes and probability of **sterilization** failure. When the patient has considered and accepted the risks of regret or failure, the physician can provide information about operative approaches, including a review of the possible complications from both the operation and the anesthesia. The patient should be informed about the advantages and disadvantages of local and general anesthesia, pain likely to be associated with the operation, and possible complications, including damage to organs or major vessels, infection, and subsequent ectopic pregnancy. The patient should be informed of her need for adequate postoperative care and support, and she should plan accordingly.

The patient should be given an opportunity to ask questions about the procedure. Both this discussion and the fact that the patient was given the opportunity to ask questions should be noted in the patient's record by the physician. All this is best accomplished at a preoperative visit scheduled far enough in advance of the operation to allow the patient ample time to weigh the factors involved in the decision. Physicians should be aware of state laws or insurance regulations that may require a specific interval between obtaining consent and performance of **sterilization** procedures. State law may mandate the use of special consent forms. Written informed consent should be obtained following counseling in a relaxed and unpressured environment. It is best not to obtain consent concurrent with labor or an abortion procedure because these events are associated with stress and a high incidence of regret of **sterilization**.

Components of Presterilization Counseling

Alternative methods available, including male **sterilization**

Reasons for choosing **sterilization**

Screening for risk indicators for regret

Details of the procedure, including anesthesia with attendant risks and benefits

The permanent nature of the procedure and information on reversal

The possibility of failure, including ectopic pregnancy

Post tubal ligation physiology, including the possibility of unrelated change in menstruation

The need to use condoms for protection against sexually transmitted diseases and human immunodeficiency virus infection if at risk of exposure

Answers to all questions to the satisfaction of the patient

Completion of informed consent document

Modified from Pollack AB, Soderstrom RM. Female tubal sterilization. In: Gerson SL, Derman RJ, Tyrer LB, eds. Fertility control and ed. London, Ontario: Guide Publishers, 1994:293-296.

Patients should be advised that female and male **sterilization** offer no protection against sexually transmitted diseases (STDs) such as human immunodeficiency virus (HIV) infection. Patients should be encouraged to use condoms or have their partners use condoms when they are at risk of exposure. In the United States, studies indicate that **sterilized** women with risk factors for STDs have low rates of condom use and infrequently attend clinics for preventive reproductive health services (6, 7).

Tubal Sterilization

Timing

Tubal **sterilization** can be performed postpartum, postabortion, or as an interval procedure (unrelated in time to a pregnancy). The timing of the procedure will influence both the surgical approach and the method of tubal occlusion used.

Postpartum **sterilizations** are performed at the time of cesarean delivery while the abdomen is open or following a vaginal delivery using a 2-5-cm subumbilical minilaparotomy incision. The subumbilical minilaparotomy approach allows for easy entry into the abdomen and access to the tubes because the anterior abdominal wall is thin just below the umbilicus over the fundus. It is best to perform postpartum minilaparotomy before the onset of significant uterine involution but following full assessment of maternal and neonatal well being. The likelihood of postpartum hemorrhage in multiparous women subsides after the first 12 hours postpartum. Postpartum minilaparotomy may be performed safely and comfortably using local anesthesia with sedation or regional or general anesthesia.

Postabortion **sterilizations** can be performed safely following uncomplicated spontaneous or induced abortion. Following a first- trimester abortion, laparoscopic **sterilization** or minilaparotomy using a suprapubic approach are both acceptable. In either case, a single anesthetic for the abortion and the **sterilization** may be used to avoid additional risk. Following a second-trimester abortion, minilaparotomy via a small midline vertical incision at the level of the fundus can be used safely. Open laparoscopy or the Hasson cannula may be used, thereby avoiding the risk of perforation of the soft, enlarged uterus associated with introduction of the laparoscopic trocar. Alternatively, an interval procedure can be performed once complete uterine involution has occurred.

Tubal **sterilization** can be performed as an interval procedure at any time during the menstrual cycle. Although performance of the **sterilization** procedure during the patient's estimated follicular phase and confirmation of patient use of a highly effective method of contraception before **sterilization** will reduce the risk of luteal phase pregnancy (a pregnancy diagnosed after **sterilization** in which conception occurred before **sterilization**), highly sensitive pregnancy testing will further reduce the risk. A same- day presterilization urine test capable of detecting human chorionic gonadotropin levels as low as 20 mIU/ml or a qualitative serum assay for the beta subunit of human chorionic gonadotropin will suffice (8). Tests this sensitive will allow for pregnancy detection as early as 1 week after conception. Performance of dilation and curettage concurrent with all interval **sterilizations** as a routine practice is not recommended on the basis of effectiveness, cost, and morbidity (9). Interval **sterilization** is usually performed using laparoscopy or minilaparotomy with local, regional, or general anesthesia. Transvaginal approaches have been described, and transcervical hysteroscopic approaches are being investigated.

Surgical Approach

Laparoscopy

Modern laparoscopy was first developed in Europe in the 1960s and became a popular method for direct visualization of the abdominal and pelvic organs. In the 1970s, it was introduced in the United States for tubal **sterilization**. In 1987, approximately one third of all tubal **sterilizations** in the United States were laparoscopic procedures. Most of these were performed under short-acting, general anesthesia in an outpatient setting.

In the United States, closed laparoscopy is used more often than open laparoscopy. In laparoscopic-**sterilization**, an endoscope is inserted through a small incision made just below the umbilicus. Closed laparoscopy is performed through a small subumbilical skin incision just large enough to admit a sharp trocar. The trocar is used to puncture the abdominal wall, gaining entry into the peritoneal cavity blindly. Open laparoscopy is performed through a 1.5-cm semilunar or vertical subumbilical incision made through the

layers of the abdominal wall until the peritoneal cavity has been entered under direct visualization (10).

Advantages of laparoscopy over other surgical approaches for **sterilization** include the opportunity to inspect the abdominal and pelvic organs, barely visible incision scars, and a rapid return to full activity for the patient. The disadvantages of laparoscopic **sterilization** include the cost and the fragility of the equipment, the special training required, and the risk of bowel, bladder, or major vessel injury following insertion of the needle or trocar.

With special training and experience, both closed and open laparoscopy can be performed with local anesthesia while maintaining a high level of patient comfort. Small studies have indicated that many women prefer the use of local anesthesia for **sterilization** procedures (11).

Minilaparotomy

The minilaparotomy approach may be performed by using local anesthesia with sedation, regional anesthesia, or general anesthesia. In contrast to laparoscopy, minilaparotomy requires only basic surgical instruments and training. Minilaparotomy is performed by using a 2-3-cm incision placed in relation to the uterine fundus. For interval **sterilization**, a uterine manipulator may be used to bring the uterine fundus toward the incision. For women undergoing either laparoscopic or minilaparotomy procedures with local anesthesia, placement of a paracervical block before insertion of the uterine manipulator reduces discomfort (12). Although most surgeons prefer to perform tubal occlusion using suture ligation and excision techniques, clips or rings may be applied through the minilaparotomy incision. With minilaparotomy, a segment of the tube can be removed for pathologic confirmation that both tubes were **sterilized**.

Methods of Occlusion

Electrocoagulation

Electrocoagulation for tubal occlusion is used exclusively with laparoscopic **sterilization**. Unipolar electrocoagulation with or without tubal excision was the first laparoscopic method of tubal occlusion. However, because uncommon but serious complications, including thermal bowel injury, were reported, bipolar coagulation was introduced and is now the most commonly used laparoscopic method in the United States. Bipolar coagulation also results in a more localized injury to the fallopian tube than does the unipolar method. Therefore, to maximize its effectiveness, at least 3 cm of the isthmic portion of the fallopian tube must be completely coagulated. Adequate coagulation requires sufficient energy of 25 W delivered in a cutting waveform (13). Use of a current meter, rather than a visual endpoint or a defined period of time, more accurately indicates complete coagulation.

Mechanical Methods

Mechanical occlusion devices commonly used in the United States include the silicone rubber band (Falope ring) and the spring-loaded clip (Hulka-Clemens clip). A new titanium clip lined with silicone rubber (Filshie clip) has been widely used in Great Britain with low reported failure rates (14, 15).

Special applicators are necessary for each of the mechanical occlusive devices, and each requires skill for proper application. The band can only be applied to a fallopian tube that is sufficiently mobile to allow it to be drawn into the applicator. Both types of clips should be applied perpendicular to the long axis of the proximal isthmus of the fallopian tube. Both types of clips and the silicone rubber band are most likely to be effective when used to occlude a normal tube. Tubal adhesions or a thickened or dilated fallopian tube increase the risk of misapplication and subsequent failure (16).

All of the mechanical methods of tubal occlusion destroy much less oviduct (about 5 mm for clips and 2 cm for rings) than do electrocoagulation methods. Therefore, if reversal is attempted, there is a greater chance of success.

Ligation Methods

Tubal occlusion at the time of cesarean delivery, laparotomy for other indications, or minilaparotomy is usually performed by using ligation techniques. A variety of techniques have been well described (17). Care should be taken to excise a sufficient section of fallopian tube to ensure complete transection of the tubal

lumen.

Efficacy

Failure

Precise failure rates for each method of tubal occlusion and long-term cumulative failure rates have been difficult to measure because of the methods' high effectiveness rates. A generally accepted failure rate of less than 1% is based on combined small studies in which different occlusion methods were used (18). Preliminary findings from the U.S. Collaborative Review of **Sterilization** indicate that cumulative failure rates are higher than expected, with significant differences between methods (19). The risk of failure persists for years after the procedure and varies by method of tubal occlusion and age. In a total of 143 **sterilization** failures, cumulative 10-year probabilities of pregnancy were highest after spring-loaded clip **sterilization** (36.5 per 1,000 procedures) and lowest after unipolar coagulation (7.5 per 1,000) and postpartum partial salpingectomy (7.5 per 1,000). The cumulative risk of pregnancy was highest among women **sterilized** at a young age with bipolar coagulation (54.3 per 1,000) and spring-loaded clip application (52.1 per 1,000). It is important to note, however, that in another study of **sterilization** failures, all spring-loaded clip failures were found to be due to misapplication (16).

Fecundity declines significantly after the age of 35 years. In one study, patients younger than 35 years were 1.7 times more likely to become pregnant following **sterilization** than women over the age of 35 years (20). In another study, among women 18-27 years of age who underwent bipolar coagulation, 2.8% became pregnant between 5 and 10 years after the procedure (19).

Pregnancies after **sterilization** may occur without any technical error. Technical error leading to failure occurs less frequently with minilaparotomy regardless of the occlusion method used (21). In one study, the location of the suture on the ligated tube affected estimated minilaparotomy failure rates, which were approximately 3% in 3 years for fimbriectomy with infundibular ligation, approximately 1.7% for ampullary ligation, and approximately 0.34% for isthmic ligation (20).

Ectopic Pregnancy

When **sterilization** failure occurs, the subsequent pregnancy is more likely to be ectopic than intrauterine. The degree of increased risk depends on the occlusion method used. The results of several reports suggest that over half of the pregnancies that occur after electrocoagulation **sterilization** procedures may be ectopic (22, 23). If an ectopic pregnancy occurs, the physician should evaluate both proximal tubes and manage any acute problems that are present.

Complications

In the United States, female **sterilization** has a mortality rate of 1-2 deaths per 100,000 procedures (24). Complications of general anesthesia are the leading cause of death from tubal **sterilization**. Other causes include sepsis and hemorrhage. Between 1977 and 1981, most of those deaths from sepsis resulted from thermal bowel injury following unipolar electrocoagulation, while most of those deaths from hemorrhage followed major vessel lacerations associated with abdominal entry for laparoscopic **sterilization** (25).

Studies in the United States indicate that women undergoing interval minilaparotomy are at approximately twice the risk of having any complication than are women undergoing interval laparoscopic **sterilization**. However, women who undergo minilaparotomy often have medical risk factors, including certain cardiac and pulmonary problems, that are contraindications to laparoscopy and therefore are intrinsically at greater surgical risk (26, 27).

Late Sequelae

The long-term health effects of tubal **sterilization** on menstrual pattern disturbance, pelvic pain, and the need for pelvic surgery are controversial. Early studies of menstrual disturbance following **sterilization** failed to account for confounding variables such as presterilization use of hormonal contraceptives that generally mask underlying menstrual dysfunction. Most recent prospective studies that account for these factors have found little or no difference in menstrual function between women before and after **sterilization**, or between **sterilized** women and nonsterilized control subjects in the first 2 years of follow up. Findings from reports

that include follow up for more than 2 years have been less consistent, yet no single method of occlusion, regardless of the amount of tubal destruction, has been associated with an increase in risk for poststerilization menstrual disturbance (28).

Two studies have evaluated the likelihood of hospitalization for menstrual disorders in women who have undergone **sterilization**. A U.S. population-based cohort study showed an increased relative risk of 1.6 (95% confidence interval of 1.3-2.1) for hospitalization for menstrual disorders compared with a control group of wives of men who have had vasectomies (29). Follow up of a large British cohort for 6 years failed to identify a significant increase in risk (30).

Some **sterilized** women may be more likely to undergo subsequent hysterectomy. Women who have been **sterilized** before age 30 have a higher risk of a hysterectomy than women **sterilized** after age 30. This risk has not been related to an increase in menstrual disturbance or the extent of tissue damage based on the method of occlusion used (31).

Ovarian Cancer

In several older studies, an inverse relationship between tubal occlusion and subsequent ovarian cancer has been found, although the strength of this relationship has varied widely (32, 33, 34). A controlled, prospective study reported a reduced risk of ovarian cancer among women who had tubal occlusion or hysterectomy (35). The study monitored 77,544 women for 12 years. For those women who had a tubal ligation, the relative risk of ovarian cancer was 0.33. The reduced risk persisted after the investigators controlled for risk factors such as smoking and protective factors (eg, use of oral contraceptives). Cases of reported ovarian cancer, identified within the first 4 years after **sterilization**, were excluded to eliminate possible screening bias (32, 33).

Pelvic Inflammatory Disease

It has long been believed that tubal **sterilization** protects against pelvic inflammatory disease. This would seem to make intuitive sense, as this condition is thought to be caused by the ascent of bacteria through the cervix, uterus, and fallopian tubes and into the peritoneal cavity. This protection is, however, not absolute. Case reports of pelvic inflammatory disease and tuboovarian abscess in women who have undergone **sterilization** are rare but do exist in the literature (36, 37).

Sterilization in Men

Vasectomy performed as an outpatient procedure has been popular in the United States since 1965. More than 5 million men in the United States have had a vasectomy (38). When compared with tubal **sterilization**, vasectomy is safer, less expensive, and equally as effective. In the United States, urologists, general surgeons, and family physicians perform vasectomy procedures in their offices using local anesthesia.

Traditionally, vasectomy was performed through two incisions in the scrotum, one overlying each vas deferens. The incisions were then closed with a suture. In 1985, the no-scalpel vasectomy technique was introduced (39). This method makes use of two specially designed instruments: one allows the vas to be fixed externally, while the second is used to puncture the scrotal skin without using a scalpel (40). The technique was developed to increase acceptability of vasectomy by reducing the apprehension related to making an incision on the scrotum (41, 40). It reduces the already low rate of minor complications (less than 3%) seen with traditional vasectomy, such as wound hematoma and infection (42).

Both traditional and no-scalpel vasectomy use the same methods to occlude the vas. These include excising a segment of the vas and sealing the ends via ligation, electrocoagulation or thermocoagulation, or clips. To decrease the incidence of recanalization, some surgeons further separate the severed ends by folding them back on one another or burying one end in the scrotal fascia.

Pregnancy rates following vasectomy are less than 1% in most studies and usually result from failure to occlude the correct structure, unprotected intercourse too soon after the operation, or spontaneous recanalization. Unlike tubal occlusion in women, vasectomy is not immediately effective: about 3 months or 20 ejaculations are needed to flush the vasa of viable sperm. Postvasectomy semen analysis should be performed to determine the effectiveness of the procedure.

The possibility of long-term side effects from vasectomy has received considerable attention. Nine separate

epidemiological studies in men have failed to show a relationship between atherosclerosis and vasectomy (43). An original study in monkeys that suggested such a relationship has not been confirmed (44, 45). Other consequences of vasectomy have been suggested, but none has been proven. In addition, several studies report that in the United States, men who have chosen vasectomies are often healthier than control counterparts (46, 47).

In Western countries, white, upper-middle-class men are more likely to choose vasectomy and are also the group more likely to have testicular cancer. A study of nearly 74,000 men who have had vasectomies showed the incidence of testicular cancer in this group to be no higher than that of the general population (48). It also showed that vasectomy does not accelerate the growth of preexisting testicular tumors.

In 1993, researchers published the first large cohort studies to show a weak but statistically significant increased risk for prostate cancer in a subgroup of men at least 20 years after vasectomy (49, 47). Two subsequent studies have failed to support these findings (50, 51).

The U.S. National Institutes of Health convened a group of experts in 1993 to review the published reports on prostate cancer. The committee found that although additional research into a possible causal relationship between vasectomy and prostate cancer should be conducted, a change in the current practice of vasectomy was not warranted. The National Institutes of Health made the following recommendations (52):

- Providers should continue to offer vasectomy and perform the procedure
- Vasectomy reversal is not warranted to prevent prostate cancer
- Screening for prostate cancer should not be any different for men who have had a vasectomy than for those who have not

Summary

Sterilization provides a safe and effective contraceptive method. Both female and male **sterilization** have few long-term sequelae. Several new methods of transcervical **sterilization** are under development, but laparoscopy and minilaparotomy are likely to remain the most popular methods of female **sterilization**.

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Issues in Brief

Family Planning Improves Child Survival and Health

Babies who survive and children who enjoy good health are universal humanitarian goals. Strategies to advance these goals in developing countries include both direct investments in health and nutrition programs and the increased availability of family planning services. These two strategies complement each other, and should be viewed together. Especially in times of fiscal austerity and reduced international assistance, they should not be pitted against each other in competition for scarce funds.

The basic conditions necessary for newborns to survive and for children to flourish are no secret. The ideal would be for all babies to be born to mothers who are in good health, who have obtained adequate prenatal care and who have access to the health facilities necessary for a safe delivery. Also needed are sufficient breastfeeding, good nutrition after weaning, hygienic living conditions—especially clean water and modern sanitation—and medical care that includes immunization against childhood diseases.

But two other, related factors also contribute to improved child health and survival in developing countries. These are smaller families and the use of methods of contraception that allow couples to plan their families. When women can plan when and how many children to have, the number of "high-risk" pregnancies and births is reduced, and infant and child health and survival improve.

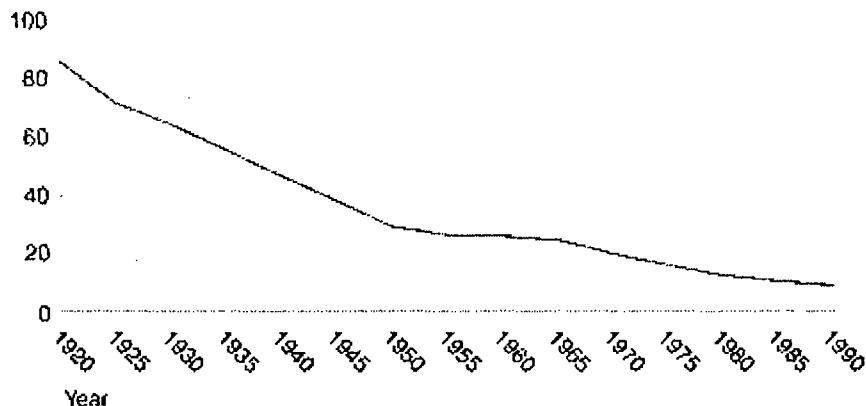
Because the conditions that enhance babies' health and chances of survival can be found in most of the developed world, the high infant mortality rates of the past have largely disappeared in the West. In France, Japan and the United States, for example, fewer than 10 babies die for every 1,000 live births. Thus, for most Americans, the death of a baby is a rare event.

Yet some older Americans can remember when infant deaths were as common in the United States as they are currently in many parts of the developing world (Chart A). In 1920, the U.S. infant mortality rate was as high as Nigeria's is today (87 infant deaths for every 1,000 live births; Table 1, column 1). In 1965, it still equaled the current rate of 25 deaths per 1,000 in Sri Lanka, and in inner-city communities particularly, the rate remains close to that level.

chart a
U.S. Infant Mortality

In the 1920s, one of every 20 babies died before their first birthday; in the 1990s, fewer than one in 100 do so.

Infant deaths per 1,000 live births



Source: National Center for Health Statistics, Vital Statistics of the United States, 1991: Vol. II—Mortality, Part A, U.S. Government Printing Office, Washington, D.C., 1996

table 1
Influencing Infant Survival

Country and year	Infant mortality rate	% of births less than 24 months apart	% of births unplanned	If want no more births, % not using effective method
Sub-Saharan Africa				
Botswana, 1988	38	6	53	65
Burkina Faso, 1992-1993	94	9	24	92
Burundi, 1987	74	9	24	97
Cameroon, 1991	64	6	20	84
Cen. Afr. Rep., 1994-1995	97	11	23	92
Cote d'Ivoire, 1994	89	7	28	93
Ghana, 1993	66	5	43	86
Kenya, 1993	62	13	51	62
Liberia, 1986	144	10	u	86
Madagascar, 1992	93	16	23	90
Malawi, 1992	135	11	41	85
Mali, 1987	105	9	14	98

Namibia, 1992	57	7	33	49
Niger, 1992	123	15	13	95
Nigeria, 1990	87	8	11	89
Rwanda, 1992	85	13	49	81
Senegal, 1992– 1993	68	11	28	90
Tanzania, 1991– 1992	92	6	22	85
Togo, 1988	77	6	39	95
Uganda, 1996	81	8	28	87
Zambia, 1992	107	6	32	83
Zimbabwe, 1994	53	5	42	57
North Africa, Middle East				
Egypt, 1992	62	12	34	45
Morocco, 1992	57	10	33	56
Sudan, 1989– 1990	70	10	23	90
Tunisia, 1988	48	16	32	49
Asia				
Bangladesh, 1993–1994	87	6	32	51
India, 1992– 1993	79	10	23	61
Indonesia, 1994	57	6	17	41
Pakistan, 1990– 1991	86	20	21	81
Philippines, 1993	34	14	44	68
Sri Lanka, 1987	25	14	36	45
Thailand, 1987	35	12	31	26
Turkey, 1993	53	11	31	61
Latin America & the Caribbean				
Bolivia, 1993– 1994	75	11	54	84
Brazil, 1996	39	10	47	27
Colombia, 1995	28	11	45	42
Dominican Republic, 1991	43	16	38	33
Ecuador, 1987	57	14	35	58
El Salvador, 1985	67	7	49	40
Guatemala, 1987	73	12	26	67
Mexico, 1987	47	14	51	45

Paraguay, 1990	34	12	23	58
Peru, 1991–1992	55	11	56	66
Trinidad & Tobago, 1987	28	16	35	53

Notes: u=unavailable. Most data for columns 1–3 refer to all births in the five years before the survey. However, data on birthspacing for about one-third of countries are for 10 years before the survey. In addition, data on unplanned births for Burundi, Namibia, Uganda, Sudan and Mexico refer only to the last birth in the previous five years. Source: All data are from the Demographic and Health Surveys.

We have known for some time that better timing and spacing of pregnancies improves child health and survival. Large-scale studies in Western Europe and North America, published in the late 1970s and early 1980s, confirmed the beneficial effects that planned and timely childbearing have on child survival.¹ More recent evidence from developing countries also compellingly links improved child survival with smaller family size and well-timed pregnancies.²

This Issues in Brief will show how family planning can lead to significant improvements in the survival of newborns and the health of small children. Because women who use contraceptive methods can choose when to become pregnant, they are better prepared than women whose pregnancies are unexpected to seek care for themselves during pregnancy, and able to time their pregnancies to achieve the best situation for the infant.

High-Risk Pregnancies

Pregnancies may have a high risk of a poor or tragic outcome if they occur shortly after a birth, are among very young mothers or women past their childbearing prime, or are among women who have already had many births.³ In addition, high-risk pregnancies increase the mother's risk of dying in childbirth, and when the mother dies, her newborn's risk of dying during its first year of life is also increased.

The ways in which ill-timed pregnancies raise the mortality risks for babies are not fully understood. Most experts agree that the causes are primarily biological, even though social factors also play a role. A mother's age, the number of births she has already had and the spacing of those births all affect her health and her ability to carry a subsequent pregnancy safely to term.

Many high-risk pregnancies end in the birth of premature or very low birth weight babies, and such infants often fail to thrive, or lack the resilience needed to overcome the many threats to survival they may face during the first days and months of life. The early weaning that occurs if a mother quickly becomes pregnant again exposes the still-fragile infant to a number of infectious organisms through its intake of water and food rather than breastmilk.

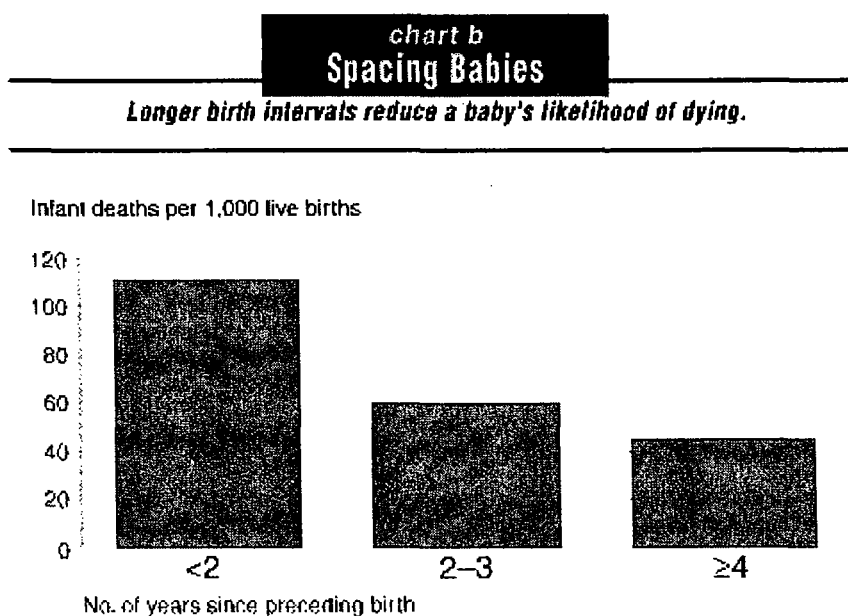
In some instances, newborns face more than one risk-enhancing situation: Some older women giving birth have already had several children; some women with large families have had many pregnancies in rapid succession; and some adolescent mothers not only are physically immature, but are giving birth for the second or third time.

In addition, many women in the developing world whose pregnancies are high-risk for

biological reasons also are at risk for social and economic reasons. They often are impoverished, and many live in unsanitary housing, are malnourished and have little education. And many women receive little or no medical care during pregnancy or when they give birth. For these reasons, disentangling the complex web of biological, social, economic and demographic factors that influence rates of child survival is difficult.

Closely Spaced Births

Babies born less than two years apart are much more likely to die than those born after a longer interval, as Chart B shows. This is a serious problem in developing countries where a substantial minority of births occur within less than 24 months of a previous one. Column 2 of Table 1 indicates that closely spaced births account for one in five of all births in Pakistan; one in six in the Dominican Republic, Madagascar, Niger, Tunisia, and Trinidad and Tobago; one in seven in Ecuador, Kenya, Mexico, the Philippines, Rwanda and Sri Lanka; and around one in 10 in another 16 of the 45 developing countries listed.



Source: see reference 2; averages are based on 45 *Demographic and Health Surveys*.

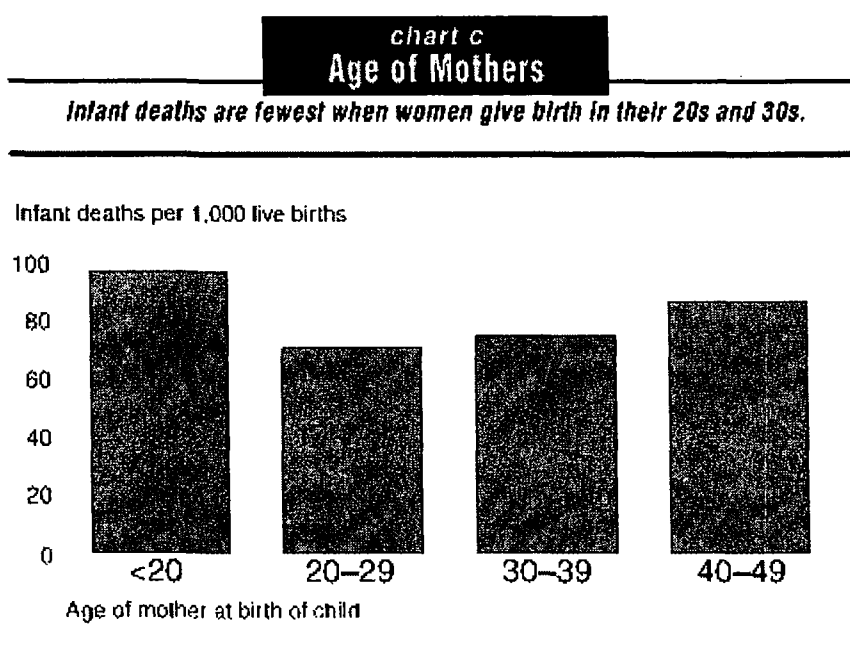
Closely spaced births present a risk to the health of all three family members involved: the mother herself, who does not have sufficient time to regain her strength after delivery; the initial child, who often has to be weaned early; and the baby born subsequently, who is likely to be premature or low-birth-weight. If all births occurring within less than two years of each other could be more widely spaced, one in four infant deaths in developing countries might be prevented.⁴

Some traditional childbearing practices have helped to ensure lengthy intervals between births. In a number of societies, for example, women have breastfed for long durations. At the same time, cultural taboos often require a lactating woman to abstain from sexual relations. Both sexual abstinence and the lengthy duration of breastfeeding have served to lengthen the interval between successive pregnancies. But as these practices become less common than in the past, the incidence of closely spaced births is likely to increase.

As populations everywhere become more urbanized, as commercial infant formulas become more accessible and as women of childbearing age work away from the home in increasing numbers, both the average length of time babies are breastfed and the once common practice of sexual abstinence after a recent birth are declining in many countries. If women who stop breastfeeding and resume sexual relations do not immediately start to practice some form of contraception, they will soon be at risk of becoming pregnant again.

Age of Mothers

Throughout the developing world, babies born to women younger than 20 are, on average, one-third more likely to die than infants born to women in their 20s and 30s (see Chart C). This is mostly because babies born to very young mothers are more likely to be premature, to be low-birth-weight and to suffer from complications at the time of delivery. And many adolescents do not know how to obtain or cannot afford good prenatal and delivery care. In addition, teenage births are likely to be first births, and first births always carry a higher risk than subsequent births.



Source: G.T. Bicego and O.B. Ahmad, 1996 (reference 2), Chart B; averages are based on 40 Demographic and Health Surveys.

The link between early childbearing and lower rates of infant survival in developing countries has serious implications. One in five women aged 20-24 report having had their first child before their 18th birthday, and two out of five report doing so before they were 20.⁵ This high incidence of teenage childbearing is partly because even when adolescents want to prevent pregnancy, they often face special problems in obtaining the contraceptive products or services that would enable them to do so.

In addition, babies born to women older than 40 are at somewhat greater risk of dying in infancy than those whose mothers are in their 20s and 30s. To compound the problem, older women often have several children already, and babies born after the mother has already had a number of children are also more likely to die in infancy than babies whose mother has had only one or two previous births. Further, in the developing world, many older women with

large families are in poor health: They often suffer from such problems as anemia, poor nutrition, cardiovascular disease or uterine prolapse.

For these reasons, helping older women avoid unwanted pregnancy improves child survival. Indeed, high levels of contraceptive sterilization in Latin America (mostly among women in their 30s or older who have had all the children they want⁶) is likely to be one reason for the overall lower infant death rates in Latin America compared with those of Asia and Sub-Saharan Africa (Table 1).

Unplanned Pregnancies

Many women in developing countries acknowledge—even after a new baby is born and part of the family—that they did not plan to have that child. The proportion of births that are reported as unplanned ranges from one-quarter to one-half in most countries (Table 1, column 3). This is troubling because there is some evidence—although it is mostly based on the experience of developed countries—of a link between whether parents wanted a child and its survival and well-being.⁷

In developed countries, women who plan to become pregnant and want a child tend to recognize that they are pregnant soon after conception. Partly because of this earlier awareness, they visit a doctor sooner and generally take better care of themselves during pregnancy than women with unwanted pregnancies. Women with wanted pregnancies are also likely to receive more consideration, support and care from family members. A review by the U.S. Institute of Medicine of the research on this topic concluded that "the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development."⁸

In developing countries, there is less evidence that a baby's safe delivery and healthy growth is linked to whether the pregnancy was a wanted one. In addition, prenatal, maternal and child health services are often not widely available or are of poor quality, and poverty sharply limits how well a family can take care of infants and children who are in poor health.

Yet there is little reason to believe that the degree to which a baby is wanted would not have some effect on women's care of themselves during pregnancy and of their newborns subsequently. One study on Indonesia, Korea and the Philippines demonstrates that even after factors such as the parents' education and economic level and the availability of health clinics are taken into consideration, babies are more likely to suffer from acute respiratory infections and severe diarrhea if the pregnancy was unwanted than if it was wanted.⁹

Understanding the Danger

Most women understand the dangers of having children at closely spaced intervals, of having large numbers of children and of having children late in their reproductive years—the three major biological factors associated with high-risk pregnancies.

When married women in developing countries who already have four children are asked if they would like to have more, about eight out of 10 say no; so do half of women with fewer children.¹⁰

Even among women who say they want another child, the vast majority want to delay their

next pregnancy. Their preferred interval between births is 3–5 years in all regions of the world.¹¹ If women were able to achieve the intervals they want between pregnancies, fewer babies would die in infancy.

But many women who say they want to stop having children altogether or to delay their next pregnancy are not using the contraceptive methods that would help them achieve these goals. In the countries of Sub-Saharan Africa, 57–98% of women who want no more children are not using an effective family planning method (Table 1, column 4). Nor are about half of women who want no more children in most countries of Asia and Latin America.

A Crucial Combination

Family planning services that help women avoid high-risk and unwanted pregnancies can contribute to improvements in infant and child health even in the poorest of countries. The impact of family planning is probably greatest when it helps women space births at healthy intervals, avoid having large numbers of children, and prevent unwanted pregnancies, especially in their later childbearing years.

Programs designed to encourage and enable women to avoid giving birth in their teenage years would also reduce infant mortality rates. However, this requires raising the average age at which most women marry or encouraging young women to postpone their first pregnancy—both difficult goals.

Nevertheless, the crucial contribution of social and economic development to better health should not be overlooked. The improved living conditions that contributed to a declining infant death rate in the United States have yet to reach many areas of the world. Millions of families in Africa, Asia and Latin America still lack clean water, decent housing, good medical services and sufficient food—basic elements needed to alleviate the causes from which most infants are dying: diarrhea, respiratory infections, malaria, measles and malnutrition.

If Americans want their tax dollars to go toward programs that would improve child health and survival in developing countries, such programs should focus on improving broad health services and economic conditions, as well as on making family planning services available to women who want and need them.

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Credits

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Menstrual Cycle Symptomatology: The Role of Social Expectancy and Experimental Demand Characteristics

PETER G. AUBUCHON, MS, AND KAREN S. CALHOUN, PhD

The purpose of this study was to examine the effects of experimental demand characteristics and social expectancies on the report and experience of presumed menstrual cycle-related moods and symptoms. Participating in the study were 18 healthy women with regular menstrual cycles who were randomly assigned to either a group told that menstrual cycle symptomatology was the focus of the study or a group to which no interest in menstrual cycle symptoms was communicated. Nine males were also included as a control group. Results indicated that women who were informed of the interest in menstrual cycle symptomatology reported significantly more negative psychologic and somatic symptoms at the premenstrual and menstrual phases than did the women and men not so informed. It appears, therefore, that the report of stereotypic menstrual cycle symptomatology is influenced by social expectancy and experimental demand characteristics.

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FACTS IN BRIEF

Title X and the U.S. Family Planning Effort

Although a woman's ability to become pregnant spans almost half her lifetime, American women today typically want only two children—a goal that, for most, is unrealistic without contraception. One of the United States' key public health goals has long been to expand access to contraceptive services to all those who need and want them, with a special emphasis on reaching those traditionally hindered in their attempts to obtain care by income or other factors, such as age or geography. This *Issues in Brief* examines the 30-year record of the nation's voluntary family planning effort, outlining its origins, describing its current structure and funding, and assessing the impact it has had in preventing unintended pregnancies, births and abortions.

Origins of the Program

Studies conducted during the 1960s showed that rates of unwanted childbearing among low-income women were at least twice as high as those among the more affluent—a phenomenon traceable in large part to inequalities in access to family planning services. By the end of the decade, a sizable, bipartisan consensus had emerged favoring government support of voluntary family planning programs as a means of expanding economic development, alleviating poverty, avoiding welfare dependency and improving the health of women and their families.

Even as this consensus was forming, Congress amended a number of federal laws to allow family planning services to be provided under existing programs. In 1965, as part of the "War on Poverty," federal funds were made available for family planning through the Office of Economic Opportunity. In 1967, Title IV-A of the Social Security Act was amended to require state welfare agencies to offer and provide family planning services to women receiving public assistance.

Then, in 1970, with broad bipartisan support, legislation establishing Title X of the Public Health Service Act was signed into law by President Richard Nixon, creating for the first time a comprehensive federal program devoted entirely to the provision of family planning services on a national basis. The new program sought to fulfill the president's promise that "no American woman should be denied access to family planning assistance because of her economic condition."

Public expenditures for family planning grew rapidly in the early 1970s, as the clinics Title X helped to create became established across the country. In 1972,

in recognition of disparities in services across states, Congress amended the Medic-aid statute (Title XIX of the Social Security Act) to mandate inclusion of family planning services in all state Medicaid programs. By the early 1980s, almost \$340 million in federal and state funds was being spent to provide family planning services to five million women at nearly 5,200 service sites.

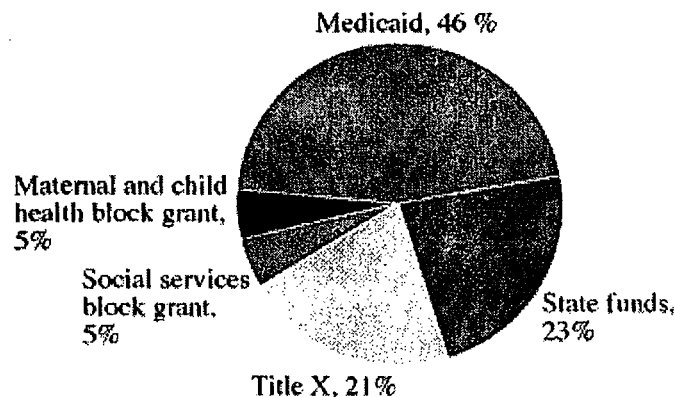
Since then, however, a persistent combination of conservative politics and fiscal pressures has forced family planning clinics to confront both budget cuts and new administrative restrictions. Despite these ongoing struggles, publicly funded agencies continue to provide services to large numbers of low- and moderate-income women and teenagers.

Sources of Funding

Public funds to provide family planning services come from diverse programs with different focuses (see Chart A). The largest source of funding is the federal-state Medicaid program. While nine in 10 family planning agencies derive at least some income from Medicaid reimbursement, few rely heavily on it. Medicaid does not fund family planning clinics or provide services directly. Instead, it is an insurance mechanism whereby federal and state governments reimburse physicians and other health care professionals for the medical services, including family planning, they have provided to eligible individuals.

Chart A: Funding Sources, 1994

Several public programs fund contraceptive services.



Many poor women are not eligible for Medicaid coverage. To qualify in most states, a woman must be single, already have a child (or be pregnant) and have an income below state requirements; nationwide, the average income eligibility ceiling is only about 46% of the federal poverty level, or approximately \$6,100 a year for a family of three.

Most poor and low-income women who do not qualify for Medicaid are dependent on publicly funded clinics for help in obtaining family planning

services. The establishment and operation of these clinics is accomplished through Title X, the only federal program dedicated solely to funding family planning and related reproductive health care services. Clinic services are also partially supported in most states with federal funds from the maternal and child health block grant and the social services block grant (Titles V and XX of the Social Security Act, respectively), but with a few exceptions, family planning services are only a small component of these broad programs.

Finally, state contributions to family planning services have grown considerably since the 1970s; 68% of family planning agencies received some support from state and local sources in 1995. Although 10 states provided no *state* funds for family planning services in 1994, some of these allocated significant proportions of their federal block-grant allotments for this purpose.

Who Provides Services?

In 1994, a total of 3,119 agencies provided organized family planning services—1,413 health departments, 159 Planned Parenthood affiliates, 534 hospitals and 1,013 other types of agencies. Together, these agencies operated 7,122 clinic sites. Of these, 44% were operated by state health departments, 13% by Planned Parenthood affiliates, 11% by hospitals and 32% by other agencies, such as independent family planning councils and community and migrant health centers.

Each clinic site served an average of 923 clients in 1994. Planned Parenthood affiliates reported serving 2,074 clients per clinic, while health department clinics, many of which are located in rural or sparsely populated areas, served an average of 681 clients annually. In the aggregate, however, both types of agencies served about the same proportion of all family planning clinic clients—30% and 32%, respectively.

Who Receives Services?

According to 1994 data, an estimated 6.6 million women receive contraceptive services annually through the network of publicly subsidized family planning providers. Overall, 30% of these clients are younger than 20, 50% are aged 20-29 and 20% are aged 30 or older. A majority of the contraceptive clients served at publicly funded agencies are non-Hispanic whites (61%), while 14% are Hispanics, 19% are blacks and 7% are Asians or of some other race. Most of the clients are poor—57% have family incomes that are below the federal poverty level, and one-third have family incomes of 100-250% of poverty. However, only one-quarter of all clients are Medicaid recipients.

While the reach of the family planning clinic network is encouraging, weaknesses in the provision of services remain. One indicator of the continuing need is shown by a 1995 National Center for Health Statistics report that U.S. women have an average of 3.3 pregnancies over their lifetimes, of which only 1.8 are wanted births. According to the report, white women average 2.8 pregnancies, 1.6 of which are wanted births; black women average 5.1 pregnancies, of which 1.8 are wanted births; and Hispanic women average 4.7

pregnancies, of which 2.6 are wanted births.¹

Services Provided

Family planning agencies provide a variety of contraceptive options—usually at lower cost than available elsewhere—along with the information and education that clients need to choose the best method for their needs. Oral contraceptives are universally available at family planning agencies, but the provision of other methods varies depending upon the type of agency. Planned Parenthood affiliates offer an average of 10 methods, while health departments and community and migrant health centers offer seven contraceptive methods, on average.

Depo-Provera, a hormonal injection that was approved for use in the United States in 1992, is now available from 96% of family planning agencies. Additional methods offered by 90% of agencies include male condoms, spermicides and the diaphragm. Some three-quarters of all agencies also offer natural family planning (periodic abstinence). Norplant is offered by 59% of agencies; the remaining six methods—the IUD, postcoital hormonal pills (emergency contraception), female condom, cervical cap, tubal ligation and vasectomy—are offered by fewer than 50% of agencies.

Besides providing contraceptive methods and related counseling, family planning clinics offer many other reproductive health services. All agencies routinely provide Pap tests, breast and pelvic exams and blood pressure measurement in the course of a woman's contraceptive visit. In addition, the vast majority of agencies provide such services as prenatal, postpartum and well-baby care; immunizations; and services under the Special Supplemental Food Program for Women, Infants and Children (WIC).

It is the policy at 94% of agencies to routinely obtain clients' sexual histories, and three-quarters of agencies routinely test for anemia. Testing for sexually transmitted diseases (STDs), urinary tract infections or pregnancy are routinely provided at some agencies; more often, however, these tests are provided only on indication or if the client requests to be tested. Routine testing for three STDs—gonorrhea, chlamydia and syphilis—is provided by 64%, 54% and 42% of agencies, respectively.

In addition, 96% of agencies routinely counsel clients regarding the risk factors for STDs and the human immunodeficiency virus, and 62% routinely provide education related to condom negotiation skills. All agencies report providing contraceptive education through individual counseling and the distribution of printed materials, and nearly nine in 10 encourage counselors to spend more time with teenagers than with other clients.

The Impact of Services

Publicly funded family planning services have been responsible for preventing large numbers of unintended pregnancies, abortions and births among low-income women, especially unmarried women and teenagers.

- Each year, publicly funded contraceptive services help women avoid 1.3 million unintended pregnancies, which would result in 534,000 births, 632,000 abortions and 165,000 miscarriages.
- In the absence of publicly funded family planning services, the number of abortions performed in the United States each year would be 40% higher than it currently is.
- Without publicly funded family planning services, an additional 386,000 teenagers would become pregnant each year. Of these, 155,000 would give birth, increasing the number of teenage births by one-quarter. Just under 50,000 of these pregnancies would end in miscarriage, and 183,000 teenagers would have abortions, increasing abortions to teenagers by 58%.
- Without publicly funded family planning services, an additional 356,000 women who have never been married would give birth each year, increasing total out-of-wedlock births by one-quarter.
- Of the 534,000 additional women who would give birth in the absence of publicly funded family planning services, 338,000 would be eligible for Medicaid coverage of pregnancy-related care; eight in 10 of these women would be eligible only by virtue of their pregnancy. Therefore, for every public dollar spent to provide family planning services, the public saves an average of \$3 in Medicaid costs for pregnancy-related and newborn care.

The data also show that public funding of family planning services prevents poor birth outcomes and improves women's overall health.

- Publicly funded family planning services increase the likelihood that pregnant women will obtain sufficient prenatal care. A study of 45,000 women who gave birth in North Carolina in 1989-1990 found that women who used family planning services in the two years before conception were more likely to begin prenatal care early and to receive adequate levels of care throughout their pregnancies.²
- A recent national study also found that publicly funded family planning services provided in 1982-1988 prevented 20,000 low-birth-weight deliveries, 6,500 infant deaths and 5,500 neonatal deaths.³
- A recently published analysis of Wisconsin's chlamydia prevention program, which includes family planning clinics as primary screening and treatment sites, found steep declines in the incidence and serious complications of the infection, such as pelvic inflammatory disease and ectopic pregnancy. Between 1987 and 1991, the incidence of new infections in women decreased by 27-50% in clinic populations.⁴

The benefits of publicly funded family planning services in the United States have long been recognized. Authorities in public health have agreed on family planning's effectiveness, not only in preventing unintended pregnancies but also in improving the health of women and children (see box, Family Planning

Benefits, below).

Benefits

- National Commission to Prevent Infant Mortality:
"Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception." *Troubling Trends: The Health of America's Next Generation, 1990*
- March of Dimes Birth Defects Foundation:

"Family planning counseling and services are essential elements of preconception and interconception care. [We] affirm that family planning should be an integral part of perinatal care to improve pregnancy outcome." *Toward Improving the Outcome of Pregnancy: The 90s and Beyond, 1993*
- Institute of Medicine Panel on Adolescent Pregnancy and Childbearing: "The availability of contraceptive services to adolescents depends heavily on public support, in particular funding through Title X, Medicaid and other federal and state maternal and child health programs. In light of the demonstrated effectiveness of contraceptive use in reducing early unintended pregnancy, continued support of these programs is essential." *Risking the Future: Adolescent Sexuality, Pregnancy, and Childbearing, 1987*
- Institute of Medicine Committee on Unintended Pregnancy: "Financial barriers [to contraception] should be reduced by increasing the proportion of all health insurance policies that cover contraceptive services and supplies,...extending Medicaid coverage for all postpartum women...and continuing to provide public funding...for comprehensive contraceptive services, especially for those low-income women and adolescents who face major financial barriers in securing such care. This last point speaks to the major role that public financing programs, such as Title X and Medicaid, have played in helping millions of people secure contraception....It is essential that such public investment be maintained." *The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families, 1995*

The Key Role of Title X

While no longer the largest funder of family planning services, the Title X program continues to be the glue that holds the national family planning system together, largely determining both its structure—through the nationwide network

of clinics—and the substance of services that are provided to low- and moderate-income women and teenagers. In 1994, 4.2 million family planning clients were served by clinics administered by Title X-supported agencies.

Because of the availability of subsidized family planning services, many women do not have to face decisions regarding an unintended pregnancy. In 1994, nearly one million unintended pregnancies were averted among women who attended Title X-funded clinics (see Table 1).

Table 1, Title X Clinics		
State	Clients served (1994)	Pregnancies averted
U.S.	4,156,850	969,700
AL	89,430	20,900
AK	6,690	1,600
AZ	33,330	7,800
AR	73,510	17,100
CA	501,080	116,900
CO	50,630	11,800
CT	49,810	11,600
DE	14,790	3,500
DC	14,540	3,400
FL	168,640	39,300
GA	169,880	39,600
HI	17,480	4,100
ID	29,590	6,900
IL	162,670	37,900
IN	77,750	18,100
IA	74,160	17,300
KS	47,720	11,100
KY	114,470	26,700
LA	58,510	13,600
ME	35,510	8,300
MD	72,210	16,800
MA	70,530	16,500
MI	127,170	29,700
MN	36,520	8,500
MS	78,920	18,400

MO	93,500	21,800
MT	28,380	6,600
NE	27,110	6,300
NV	17,400	4,100
NH	31,730	7,400
NJ	102,010	23,800
NM	40,170	9,400
NY	237,670	55,400
NC	112,680	26,300
ND	14,250	3,300
OH	141,290	33,000
OK	53,620	12,500
OR	35,130	8,200
PA	262,190	61,200
RI	13,150	3,100
SC	65,810	15,400
SD	17,070	4,000
TN	101,810	23,800
TX	233,300	54,400
UT	15,430	3,600
VT	9,240	2,200
VA	79,130	18,500
WA	88,290	20,600
WV	70,820	16,500
WI	79,050	18,400
WY	11,080	2,600

Title X is administered by the Department of Health and Human Services (DHHS), which is responsible for allocating among the 10 federal health regions the funds appropriated annually by Congress. The federal health administrator in each region receives applications from, and awards grants on a competitive basis to, public agencies and private nonprofit agencies that provide contraceptive services as well as training, technical assistance and other support.

In 1994, a total of 85 primary grantees (1-6 per state) received Title X support. Fifty-one of these were state, territorial, local or municipal health departments; 14 were independent family planning councils (regional, nonprofit umbrella agencies); seven were Planned Parenthood affiliates; and 13 were other types of community agencies, such as hospitals.

Some Title X grantees operate family planning clinics directly, distributing grant funds among their various facilities. Others allocate the money to "delegate

agencies," which operate individual clinics. Agencies providing family planning services, whether primary Title X grantees or their delegates, are diverse, community-based organizations. They include university medical centers, community action organizations, community health centers, nursing service organizations and a wide variety of nonprofit agencies, many of which are located in places where little or no other reproductive health care is available.

In 1994, nearly two-thirds of all women served by family planning clinics, 4.2 million women, obtained care at one of the 4,200 clinics receiving Title X funds. Health department sites were the most likely to receive Title X funding (78%), followed by independent clinics and Planned Parenthood sites (66% each), hospital clinics (28%) and community and migrant health centers (18%). Overall, clinics receiving Title X funds served at least 25% more clients per site than those that did not. In addition, because Title X funding is not tied to specific medical services for specific eligible clients, the agencies that received this funding were able to serve more uninsured, near-poor clients, more adolescents and more members of other special populations than were clinics that did not receive these funds.

Title X also determines the substance of the services offered to individuals. Each grantee is ultimately responsible for ensuring that its delegate agencies and the clinics they run meet the program's requirements. The law establishes a broad definition of family planning and sets standards for reproductive health care with which all providers receiving any Title X funds must comply. The Title X regulations and official program guidelines outline in great detail protocols for the provision of family planning services that comport with nationally recognized medical standards, including a mandate that patients at clinics supported by Title X be offered—on a purely voluntary, confidential basis—the full range of contraceptive methods and related counseling.

Any woman, regardless of her age, marital status or childbearing experience, may go to a Title X-funded clinic for family planning services. However, the amount each individual pays for the services she receives depends on her income. If she is very poor (her income is at or below 100% of the federal poverty level), the law requires that she receive fully subsidized services. If her income is above 250% of poverty, she must pay the full fee charged by the clinic, and if it falls in between, she must be charged for services on a sliding-fee scale.

The Title X program also supports three functions aimed at assisting clinics to respond to clients' changing needs. To foster consistently high standards in the delivery of family planning services, Title X supports centralized training in each of the 10 federal health regions and is a major source of funding for five of the nation's accredited nurse practitioner training programs. Title X specifically authorizes research to improve the delivery and efficiency of family planning services nationwide. Third, Title X requires that information be collected on the program and its clients and provided periodically to Congress.

Title X and Politics

As the one federal program devoted to the provision of family planning services,

Title X has been the focal point for much of the political wrangling over reproductive health issues.

Eliminating Title X. In 1995, Rep. Bob Livingston (R-LA) proposed eliminating the Title X program and reallocating its funds to the maternal and child health block grant and community and migrant health centers—without requiring that any of the reapportioned funds be spent to provide family planning services. He and his supporters argued that Title X should be turned over to the states to permit maximum flexibility in the provision of health care services, reviving the long-standing debate over whether responsibility for the nation's social programs should rest with the federal government or the states.

Opponents of the Livingston amendment maintained that states wishing to administer the Title X program are already free to do so under the law and that passage of the amendment would jeopardize the existing network of clinics; the 25% of U.S. counties dependent solely on family planning service providers supported by Title X would be at risk of losing their family planning providers. Moreover, because of restrictions in the maternal and child health law, 30% of the funds at most could be spent to provide family planning. In the end, the House chose to maintain Title X as a discrete health program, defeating the Livingston amendment by a vote of 221-207.

Title X and Teenagers. From its inception, Title X has required that services be made available without regard to age or marital status. Consequently, Title X-supported clinics have always provided confidential services to adolescents who request them.

This fundamental underpinning of the program was challenged in 1996, when Rep. Ernest Istook (R-OK) offered an amendment that would have required family planning providers to obtain written parental consent for most minors seeking services at Title X-funded clinics.

The issue of adolescents' ability to consent to their own health care had not been confronted to such an extent since the Reagan administration proposed new Title X regulations in 1982, which were popularly known as the "squeal rule." While citing as its legal basis a congressional mandate from the previous year that Title X-funded clinics "to the extent practicable...encourage family participation" in minors' family planning decisionmaking, the squeal rule would have gone further to *require* clinics to notify parents by registered mail of their children's visit to a family planning clinic. Although more than 40,000 letters of protest were filed with DHHS from medical, health and civic groups, the regulations were finalized in 1983. But two federal appeals court judges eventually barred enforcement, and the regulations were withdrawn before going into effect.

Proponents of the 1996 Istook amendment stated their objections to the use of federal tax dollars to fund contraceptives for their children without their knowledge. In response, the amendment's opponents pointed out that the majority of teenagers do not come to family planning clinics until they have already been sexually active for at least a year, and that creating additional delays could discourage adolescents who are trying to take responsibility for their lives by protecting themselves against unintended pregnancies and STDs.

In the end, a substitute amendment requiring Title X grantees to certify to the DHHS secretary that they encourage family participation in line with their long-standing mandate to do so prevailed by a vote of 232-193.

Title X and Abortion. From the beginning, the Title X statute has prohibited use of the program's funds for "abortion as a method of family planning." Congressionally requested investigations in the 1980s repeatedly found that all Title X-supported clinics were operating in full compliance with the law.

However, counseling regarding the management of an unintended pregnancy and referrals for requested medical and social services not offered by Title X are standard practice and are required by the program's guidelines. Nonetheless, in 1987, President Ronald Reagan ordered DHHS to promulgate new regulations that would have prohibited doctors and other health care professionals working in Title X-funded clinics from providing any abortion-related information or referrals.

The regulations generated more than 75,000 comment letters. Thirty-six state governments and a host of national health, medical and civic groups wrote in opposition to the proposed rules, expressing concern that withholding this information would violate their medical ethics and standards. Moreover, they pointed out, many of the women who depend upon Title X services often have no other source for this information.

While the legality of the so-called "gag rule" was upheld by the U.S. Supreme Court in 1991, Congress later passed legislation to overturn it. President George Bush vetoed the legislation, but a series of last-minute court orders blocked the regulations' enforcement. They were ultimately withdrawn in 1993 at the direction of President Bill Clinton.

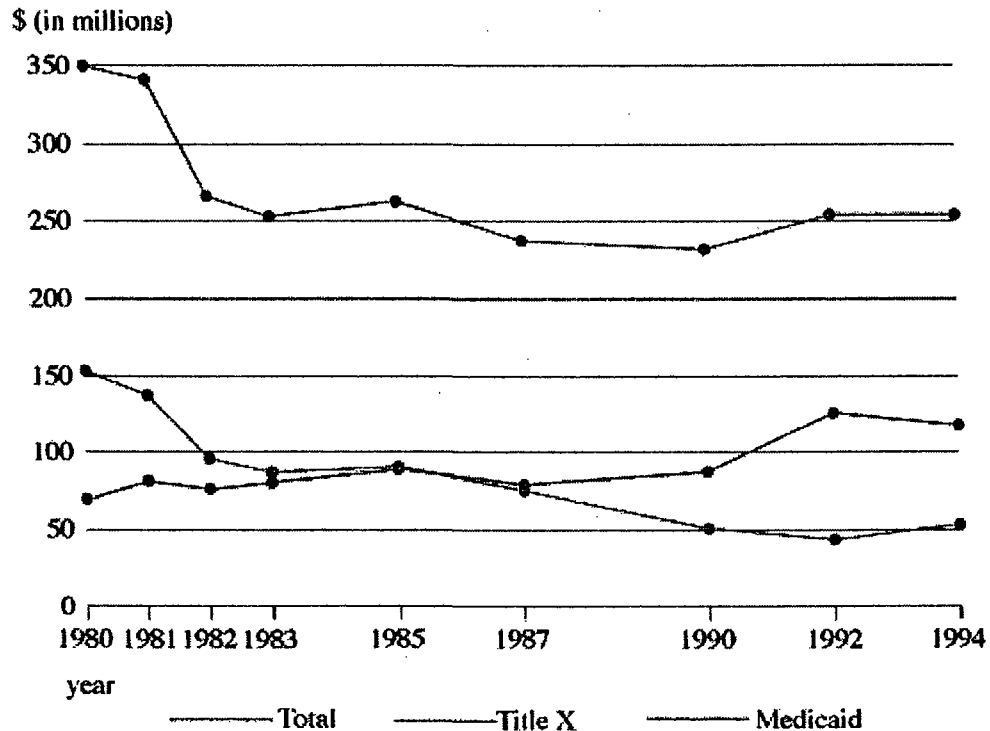
Looking Ahead

Over the last decade or so, the proportion of public funding for family planning services from different sources has shifted greatly. Of the \$715 million spent by all public sources—federal and state—to provide contraceptive services in 1994, \$332 million, or 46%, was spent under Medicaid. In contrast, the Title X program, through which \$151 million was spent for contraceptive services, accounted for only 21%.

In constant dollars—that is, dollars adjusted for inflation—Title X expenditures for contraceptive services decreased by 65% between 1980 and 1994. Despite a 70% increase in Medicaid, *total* public expenditures for contraceptive services dropped by 27% during that period (see Chart B).

Chart B: Funding Trends

Spending for family planning, in constant 1980 dollars, is down.



At the same time, the cost of providing certain family planning services, such as contraceptive supplies and related laboratory expenses, appears to have risen: Between 1991 and 1992, the average price that publicly funded clinics paid for oral contraceptives rose 42%, for example.

Furthermore, many individuals who seek reproductive health care at family planning clinics often have other health care needs. In recent years, for example, the proportion of patients coming to family planning clinics in need of screening or treatment for STDs has increased dramatically. Forty percent of all medical visits to one Title X grantee in 1990 involved testing or treatment for STDs, compared with only 10% of visits in 1980. By 1993, STD and AIDS counseling, testing and treatment constituted, on average, 26% of the contraceptive services budgets among the agencies that offered these services.

Moreover, since clients of Title X-supported clinics frequently have no other source of health care, clinics must address patients' health needs more comprehensively, by offering such corollary health services as screening for diabetes or high cholesterol levels, programming on prenatal care or smoking cessation, and counseling on domestic violence or substance abuse. All of these efforts consume additional resources, in both staff time and money, usually without extra funding from any source.

Some providers cannot absorb these additional costs without cutting back on their patient populations. Others are forced to forgo routine testing and to base treatment on examinations alone. Still others must change the nature of their services, by requiring fees or taking a higher proportion of clients who can afford to pay. For poor women seeking to prevent unintended pregnancy—particularly many of those who may be leaving the welfare rolls in light of the 1996 welfare reform law—some of these changes could present insurmountable

obstacles.

Despite growing enrollment in managed care plans nationwide, the need for the reproductive health services provided by publicly funded family planning clinics remains crucial for many low-income women, especially those who are uninsured. Even women who have some type of health care coverage continue to seek care at family planning clinics—whether or not those clinics are participating in managed care networks—because their plans do not cover the contraceptives they want or because of concerns about confidentiality.

Despite the continuing need for subsidized family planning services, some critics argue that Title X should be defunded entirely because it has failed to solve our national problems of unintended teenage pregnancy and out-of-wedlock births. Some even go so far as to claim that contraception itself is a failure, and that the provision of publicly funded family planning services has made these problems worse.

Yet incontrovertibly, contraception works: While no contraceptive, and no contraceptive user, is perfect, the fact remains that the 10% of American women at risk of unintended pregnancy who do not practice contraception account for 53% of all unintended pregnancies. Even the strongest supporters of the national family planning program readily admit that it will never, by itself, reduce the nation's unintended pregnancy rate to zero. Nevertheless, they also point out that the availability of affordable, voluntary family planning services remains the only programmatic intervention that—in a cost-effective manner—has a demonstrated ability to reduce unintended pregnancy, avert the need for abortion and improve birth outcomes and the overall reproductive health of women in the United States.

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GYNECOLOGY

A comparison of different laparoscopic sterilization occlusion techniques in 24,439 procedures

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This investigation assessed the safety and efficacy of five laparoscopic tubal occlusion techniques for female sterilization: electrocoagulation, the tubal ring via conventional and open laparoscopy, the prototype spring-loaded clip, and the Rocket clip. The 24,439 cases make up a data set collected by collaborating staffs at 64 institutions in 27 countries. The five techniques were compared with respect to six commonly evaluated parameters. Rates of surgical difficulties ranged from 2.4% to 12.5% (5.1% overall); rates of surgical complications, from 0.7% to 2.7% (1.7% overall); and rates of technical failures, from 0.6% to 1.0% (0.8% overall). Twelve-month life-table pregnancy rates were less than one per 100 woman years. Prospective data on six menstrual parameters revealed that the menstrual cycles of the majority of women were unchanged after sterilization; for those who reported a change, approximately half experienced a change in one direction and half in the other direction. For example, one half reported an increase in the amount of menstrual flow, and one half reported a decrease in the amount of flow. The reported incidence of subsequent pelvic operations was less than 1% at each long-term follow-up. These data indicate that laparoscopic sterilization is safe and effective and that none of the studied techniques has a distinct advantage. (Am. J. OBSTET. GYNECOL. 144:319, 1982.)

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We are grateful to our Executive Director, Dr. Malcolm Potts, for his useful comments on the manuscript. Various investigators in several countries have contributed data used in this analysis, and although they

are too numerous to mention individually by name, we acknowledge their efforts, without which this work would not have been possible.

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Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study

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Objective: To assess the safety, acceptability, and economy of local anesthesia and intravenous (IV) sedation versus short-term general anesthesia for laparoscopic sterilization.

Methods: We randomly allocated 125 of 150 consecutively sterilized women to either local or general anesthesia. No women were excluded, but 25 chose not to participate. The women were interviewed before surgery, and they returned a standardized questionnaire after discharge from the hospital. All laparoscopic tubal sterilizations were performed by senior gynecologists. Midazolam was used as premedication. In the local-anesthesia group, lidocaine with adrenaline was infiltrated infraumbilically and bupivacaine was applied to each tube. Midazolam and alfentanil were used as IV sedation. In the general-anesthesia group, intubation anesthesia was accomplished with alfentanil and propofol; utracurium was used for muscle relaxation.

Results: In the local-anesthesia group, operation time was shorter, perioperative discomfort was modest, and the costs of equipment were lower than in the general-anesthesia group. There was less postoperative abdominal pain and less need of analgesics, and the patients were more awake in the evening. The rise in heart rate and blood pressure were higher in the local-anesthesia group, and external oxygen was necessary to avoid apnea. Anesthetic surveillance was therefore mandatory.

Conclusions: Local analgesia was highly acceptable to the majority of patients as well as to the gynecologists. The operation time was less, postoperative recovery was quicker, and the women were less bothered by abdominal pain and sore throat. There was a substantial reduction in anesthesia costs. Anesthetic surveillance during surgery was necessary. (*Obstet Gynecol* 1993;81:137-41)

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Fact Sheet

Pregnancy-Related Mortality

- Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native women suffer a significantly higher risk of pregnancy-related mortality than non-Hispanic white women, while black women continue to have the highest risk of all of these racial and ethnic groups.
- There were 3193 pregnancy-related deaths between 1991 and 1997 in the United States. This results in an overall pregnancy-related mortality ratio (PRMR) of 11.5 per 100,000 live births.
- Hispanic women had a PRMR of 10.3 for the study period, while Asian/Pacific Islanders and American Indian/Alaska Natives had higher PRMRs, 11.3 and 12.2 respectively. In comparison, non-Hispanic whites had a PRMR of 7.3 and blacks had a PRMR of 29.6.
- The risk of a pregnancy-related death was lowest for women under the age of 30, rising after the age of 35, for all of the racial and ethnic groups where there was a large enough number to analyze.
- Place of birth, within the United States or elsewhere, was also related to the PRMR for some racial and ethnic groups. Hispanic women born outside of the United States had nearly a 50% higher PRMR than Hispanic women born within the United States.
- Women of Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native origin represented 16% of the reproductive-age population in 1997, but accounted for nearly a quarter of all of the live births in the United States. The Census Bureau projects by 2025, women of these racial and ethnic groups will make up a quarter of the women in the United States.
- A pregnancy-related death is defined as a death that occurred to women during their pregnancy or within one year after the end of the pregnancy, resulting from pregnancy complications or effects.

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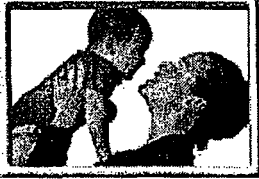


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Safe Motherhood: Promoting Health for Women Before, During, and After Pregnancy 2002

At A Glance 2002

"We as a nation must do all we can to ensure that all mothers are safe and healthy before, during, and after pregnancy. Every year, nearly 1,000 of our sisters and daughters die and hundreds of thousands of others experience medical complications from pregnancy. Death and serious illnesses due to pregnancy and childbirth shouldn't be part of the picture in the United States."

Wanda K. Jones, DrPH
Deputy Assistant Secretary for Health (Women's Health)
Director, Office on Women's Health, U.S. Public Health Service

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Safeguarding the Health of Mothers

Approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Safe motherhood begins before conception with proper nutrition and a healthy lifestyle. It continues with appropriate prenatal care, the prevention of complications when possible, and the early and effective treatment of any complications that do occur. The ideal result is a labor at term without unnecessary interventions, the delivery of a healthy infant, and a healthy postpartum period in a positive environment that supports the physical and emotional needs of the woman, infant, and family.

Deaths From Pregnancy Complications: No Decline in 20 Years

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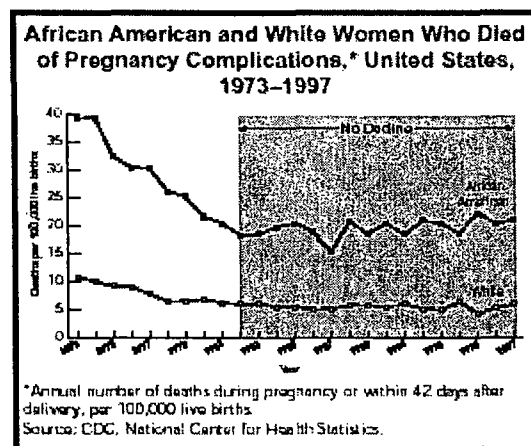
Each day in the United States, two to three women die of pregnancy complications. From 1900 to 1982, deaths from pregnancy complications in the United States declined dramatically. Since 1982, however, deaths stopped declining, and there has been no further improvement. Studies indicate that as many as half of all deaths from pregnancy complications could be prevented through broader access to health care, better quality of care, and changes in health and lifestyle habits.

The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy (heart muscle disease).

Large Racial, Ethnic, and Age Disparities

A woman’s race, ethnicity, country of birth, and age are associated with her risk of dying from pregnancy complications. For example,

- African American women are 4 times as likely to die of pregnancy complications compared with white women, and American Indian and Alaska Native women are nearly twice as likely to die.
- Asian and Pacific Islander women who immigrated to the United States are twice as likely to die of pregnancy complications as those born in the United States. Hispanic women who immigrated are 1.5 times as likely to die as those born in the United States.
- Women 35–39 years old are nearly 3 times as likely to die of pregnancy complications as women 20–24 years old. The risk of dying is even greater for women over 40.



Deaths Only Part of the Picture

More than one in three pregnant women in this country develop a pregnancy complication. The most common complications include

- Miscarriage
- Ectopic pregnancy
- Hemorrhage
- Infection
- Diabetes
- High blood pressure
- Excessive vomiting

- Premature labor
- Need for a caesarean delivery
- Depression

Childbirth remains the most common reason for hospitalization in the United States, and pregnancies with complications result in more costly hospitalizations. In the United States, hospitalizations for pregnancy complications before delivery account for more than 2 million hospital days of care each year and cost more than \$1 billion annually. These figures would be even higher if we took into account complications during or after delivery.

Economic costs are not the only concern. Pregnancy complications and deaths also cause pain and suffering. We need to learn more about how pregnancy complications affect women and their infants and families.

CDC's National Leadership and State Partnerships

The Safe Motherhood Initiative

CDC and its many partners are making major strides in safeguarding the health of mothers. Supporters of healthy motherhood include not only health departments and other federal agencies but also universities, private practices, advocacy groups, professional organizations, and businesses. In 2001, CDC and its partners

- Held the first U.S. Summit on Safe Motherhood, which brought together a broad coalition of agencies, organizations, and professionals dedicated to improving maternal health. They discussed the social, economic, and medical aspects of maternal health and called for research, policies, and coordinated action to make maternal health a national priority.
- Published *Strategies to Reduce Pregnancy-Related Deaths: From Identification to Action*. This guide helps states identify maternal deaths, expand the types of data collected about deaths, and apply the findings to protect women's health.
- Published a journal issue devoted to studies of what is unique about the experience of being an African American woman that puts her at higher risk for having a premature baby. Racism, limited health care options, and poor-quality housing are some of the problems explored.
- Expanded the Pregnancy Risk Assessment Monitoring System so that surveys of new mothers are conducted in 32 states and New York City and now cover 62% of all U.S. births.

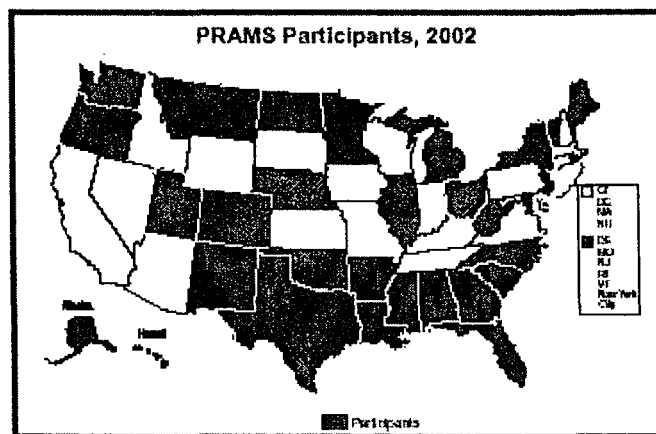
CDC works with states to translate science into quality programs. As partners, CDC and states can reduce pregnancy complications and save lives—by monitoring maternal health, conducting research, and educating people about safe motherhood.

Pregnancy Mortality Surveillance System (PMSS). Through the PMSS, CDC works with state health departments and other organizations to identify and gather information on pregnancy-related deaths. CDC uses PMSS data to examine

- Trends in pregnancy-related deaths.
- Risk factors for pregnancy-related death.
- Disparities related to race, ethnicity, and age.
- Specific conditions leading to death.

Maternal and Child Health Epidemiology Program (MCHEP). This program helps state and local health departments collect and analyze data needed to improve the health of mothers and children. CDC and the Health Resources and Services Administration (HRSA) support the MCHEP. Through the MCHEP, epidemiologists specializing in maternal and child health serve 10 states and two Indian health agencies. MCHEP also provides technical assistance and training to public health staff and sponsors conferences and Internet groups where peers can share their knowledge about maternal and child health.

Pregnancy Risk Assessment Monitoring System (PRAMS). CDC and state health departments use PRAMS to collect state-specific, population-based data on women's behaviors and experiences before, during, and immediately after pregnancy. These data identify groups of women at high risk for health problems, monitor changes in health status, and measure progress in improving the health of mothers and infants. PRAMS surveys are now conducted in 32 states and New York City.



Learning More, Making a Difference

Conducting Innovative Research

To learn more about how to improve women's health before, during, and after pregnancy, CDC supports innovative research, including the following projects:

- **Racial and ethnic differences in pregnancy complications and deaths.** One of the greatest racial gaps in public health is the fact that African American women are four times as likely as white

women to die of pregnancy complications. CDC is examining national data to find out why the risks for complications and deaths are so much greater among these women. CDC also is collaborating with researchers in North Carolina to explore whether African American women have more severe pregnancy complications than white women and whether they receive different treatment when they seek medical care for pregnancy complications.

- **Intimate partner violence among pregnant women.** Each year, up to 300,000 pregnant women in the United States are victims of intimate partner violence. Violence is more common among pregnant women than many conditions for which they are routinely screened. CDC and the American College of Obstetricians and Gynecologists developed training materials clinicians can use to screen women for violence during prenatal care visits. Moreover, CDC is funding an evaluation of a model intervention in which screening for violence is a routine part of obstetric and gynecological care. This evaluation also will help determine whether abused women who are identified through screening get the help they need.
- **Effects of high-tech infertility treatments.** In vitro fertilization and other high-tech infertility treatments are an increasingly common choice for the estimated millions of couples who face infertility each year. In 1999, more than 86,000 such procedures were performed in the United States, and over 30,000 babies were born as a result. CDC is now working with Massachusetts to study how these procedures affect the health of mothers and their infants.

Gathering Strong, Useful Data

Here are some of the ways that CDC and its partners are addressing the need for more complete and accurate information about pregnancy complications and deaths:

- Working with researchers in Oregon, Washington, and Illinois to find the best ways to identify and monitor pregnancy complications and risk factors.
- Collaborating with researchers in six cities to better understand how stress and infections affect the health of pregnant women and their babies.
- Expanding PRAMS and MCHP to more states, strengthening the states' ability to identify and address maternal and child health problems.
- Analyzing national and state data to learn more about pregnancy complications and to identify factors involved when a woman dies or almost dies of pregnancy complications.

Educating and Training Others


CDC works with many partners to share knowledge about safe motherhood. For example, CDC is

- Identifying strategies that health care providers can use to reduce pregnancy complications.
- Reporting trends in maternal and child health for states to use in program planning.
- Training public health professionals to better understand maternal

and child health problems and potential solutions.

- Working with women in Los Angeles communities to develop educational materials that will help pregnant women recognize the warning signs of preterm labor.
- Producing a *Maternal and Child Health Journal* issue highlighting the latest research on the health of women before, during, and after pregnancy.

CDC also helped to prepare *Healthy People 2010* goals that aim to dramatically improve the health and wellbeing of mothers in America over the next decade. To help the nation meet these goals, CDC will work with other federal agencies, states, nonprofit organizations, and community groups. As partners, we can make safe motherhood a reality.

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Complications of Interval Laparoscopic Tubal Sterilization

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In 1978, the Centers for Disease Control initiated a multicenter prospective study to assess the safety of the various female sterilizing operations and the ways in which they could be made safer. During the first 31 months, 3500 women who underwent interval laparoscopic tubal sterilization by electrocoagulation or Silastic banding without other concurrent operations were enrolled in the study. When a standard definition of complications was used, the overall rate of an intraoperative or postoperative complication was 1.7 per 100 women. Several patients factors increased the risk of complications twofold or more: diabetes mellitus, previous abdominal or pelvic surgery, lung disease, a history of pelvic inflammatory disease, and obesity. There was a fivefold difference in complication rates between procedures performed under general anesthesia and those done under local anesthesia. (*Obstet Gynecol* 61:153, 1983)

In 1978, the Centers for Disease Control initiated a multicenter prospective study to assess the safety of the various sterilizing operations and the ways in which they could be made safer. A planned interim analysis was done for the first 31 months of data collection, focusing on intraoperative and postoperative complications that occurred among women who underwent interval laparoscopic tubal sterilizations by electrocoagulation or Silastic banding. The authors developed a definition of standard complication categories, measured the morbidity associated with these complications, and analyzed the factors that altered the risk of complications. The rate of complications was less than 2 per 100 women; the safest procedures were those done under local anesthesia.

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Two randomized controlled trials comparing the Hulka and Filshie Clips for tubal sterilization

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Abstract

To compare the effectiveness and safety of the Filshie Clip System™ and Hulka Clip System when applied via minilaparotomy and laparoscopy, we conducted 2 multicenter randomized controlled trials of 2126 women (878 in the minilaparotomy study and 1248 in the laparoscopy study) who received either the Filshie or Hulka Clip. A physician other than the operator evaluated patients postoperatively and again at 1, 6, and 12 months after surgery. We compared the cumulative incidence of pregnancy and the frequency of safety related events for the device groups. Twenty-four month follow-up was planned for a subset of 599 women in the laparoscopy study. One woman who received the Filshie Clip and 6 women who received the Hulka Clip became pregnant within one year. The 12-month life-table pregnancy probability was 1.1 per 1000 women in the Filshie Clip group and 6.9 per 1000 women in the Hulka Clip group. The difference in the risk of pregnancy through 12 months between device groups neared statistical significance ($p = 0.06$). Among the extended follow-up subset, the 12- and 24-month cumulative pregnancy probabilities were 3.9 and 9.7 per 1000 women for the Filshie Clip group and 11.7 and 28.1 per 1000 women for the Hulka Clip group ($p = 0.16$ for comparison through 24 months). Both the Filshie and Hulka Clips are effective and safe for use in tubal occlusion. © 2000 Elsevier Science Inc. All rights reserved.

Keywords: Tubal occlusion devices; Female sterilization; Filshie Clip; Hulka Clip

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The minilaparotomy study was conducted by Milton Cordero, MD, of PROFAMILIA, Santo Domingo, Dominican Republic; Jorge Lasso de la Vega, MD, of Complejo Hospitalario Metropolitano, Panama City, Panama; Arturo Remes Ruiz of Hospital General de Veracruz, Veracruz, Mexico; John Thambu, MD, of Kuala Lumpur Maternity Hospital, Kuala Lumpur, Malaysia; and David Lim, MD, of the LPPKN National Population and Family Development Board, Kuala Lumpur, Malaysia. The laparoscopy study was conducted by Serge Louissaint, MD, of Région Sanitaire du Sud, Le Cayes, Haiti; Roberto Santiso Galvez, MD, of APROFAM Guatamala City, Guatamala; Luis Uribe, MD, of Hospital Gineco-Obstetrica, Guadalajara, Mexico; and Ilic Zigelboim, MD, of Maternidad Concepción Palacios, Caracas, Venezuela.

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Hospitalization for pregnancy complications, United States, 1986 and 1987

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OBJECTIVE: The purpose of our analysis was to provide a national overview of the magnitude of the public health burden associated with inpatient care for pregnancy complications.

STUDY DESIGN: We analyzed data from the National Hospital Discharge Survey for 1986 and 1987. We calculated ratios of hospitalizations for pregnancy complications for every 100 hospitalizations involving a birth. Standard errors for these ratios were calculated with RATIOEST, and relative ratios with 95% confidence intervals were calculated for subgroups of interest.

RESULTS: We found that for every 100 hospitalizations involving a birth, there were 22.2 nondelivery hospitalizations for pregnancy complications (14.6 antenatal complications, 7.6 pregnancy loss complications). These ratios were higher for black than for white women (relative ratio 1.4, 95% confidence interval 1.2 to 1.6). The effects of marital status, age, and insurance coverage differed between black and white women, and mean length of stay was longer for black than for white women.

CONCLUSION: Hospitalization for pregnancy complications is far more common than is widely appreciated and is more frequent among black than white women. (AM J OBSTET GYNECOL 1992;166:1339-44.)

Key words: Maternal morbidity, pregnancy complications, hospitalization, race

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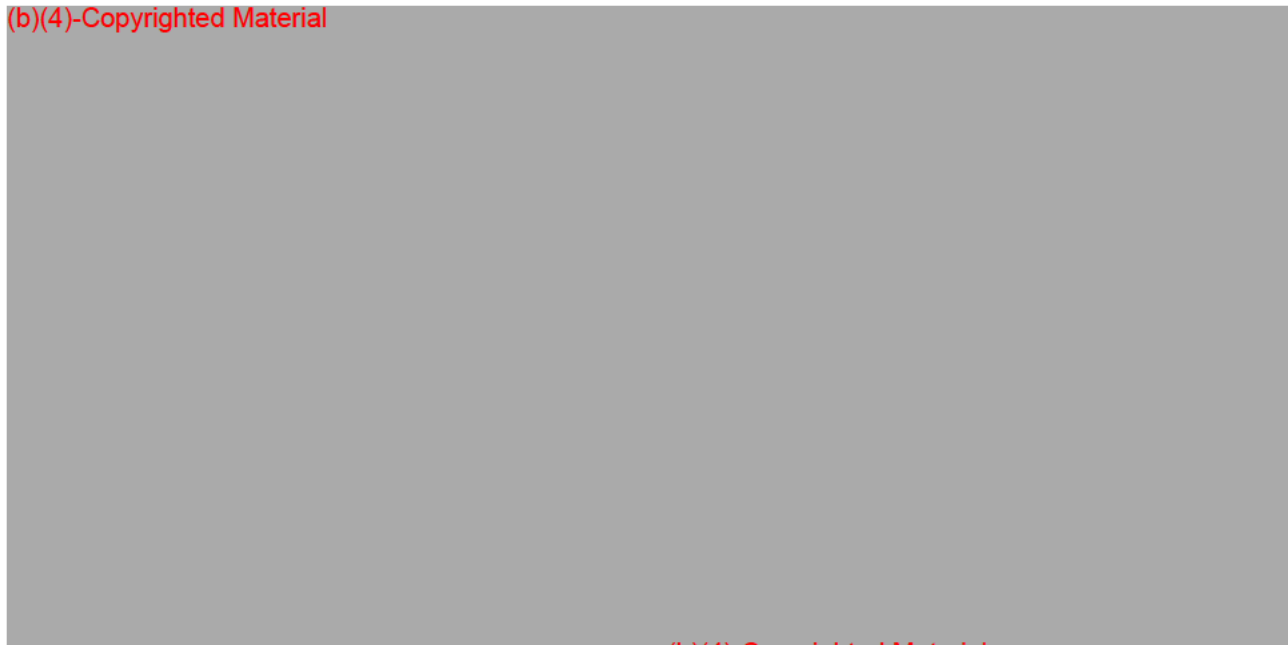
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A preliminary study of factors influencing perception of menstrual blood loss volume

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Sixty-nine women with a convincing complaint of menorrhagia took part in a double-blind treatment trial. Menstrual blood loss was measured and the subject's own perception was carefully recorded. Only 38% had objective menorrhagia with a measured loss >80 ml although 59% would qualify with an upper limit of normal of 60 ml. Overall the measured loss in the "heaviest" periods (89.6 ± 7.3 ml; mean \pm SEM) were significantly greater than that of the "lightest" periods (42.7 ± 4.7 ml; $p < 0.001$), but there were many major errors in perception by individuals. Perceived daily blood loss volume on a 4-point rating scale gave the following group means and ranges: spotting, 2.5 ml (0.1 to 15.5); light, 5.7 ml (0.1 to 63.1); moderate, 16.1 ml (0.5 to 108.6); very heavy, 22.0 ml (1.4 to 215.8); very wide individual ranges of assessment are illustrated. As a whole the group was also able to distinguish between a day-to-day volume increase or decrease, but again there were many major errors. Some subjects who experienced a reduction in measured blood loss from one day to the next actually perceived this as a large increase. Menstrual pain and duration of bleeding were not found to influence perception of blood loss volume, whereas younger subjects (26 and under) were significantly more likely than older women (37 and over) to regard a moderate loss as very heavy. There was no significant correlation between the number of pads/tampons used and the measured menstrual loss, and some individuals showed extreme variations between blood loss and pad usage. This study suggests that the only reliable assessment of menstrual blood loss volume and changes in volume in women complaining of menorrhagia is obtained by objective measurement of blood loss by a technique such as alkaline hematin extraction. (AM. J. OBSTET. GYNECOL. 149:788, 1984.)

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The prevalence and impact of pain after day-care tubal ligation surgery

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(Received 6 April 1989, accepted 23 June 1989)

Summary Empirical data from controlled studies using standardized, reliable measures on the amount and quality of pain after laparoscopic tubal ligation and the consequences of this pain on the activities of daily living are extremely scarce. In a study of 54 women admitted to a day-care unit for this procedure, validated measures were utilized to assess the incidence, intensity and duration of pain after tubal ligation (McGill Pain Questionnaire) and the impact of pain on the activities of daily living (Modified Functional Assessment Inventory). Psychological measures (Brief Symptom Inventory, Krons Health Opinion Survey, and the State-Trait Anxiety Inventory) were employed to test their use as possible predictors for pain, analgesic usage and the time taken to resume a normal activity level after tubal ligation surgery. The results showed that pain is a significant problem after tubal ligation although pain rating scores over the 7-day study period were lower than those reported after major abdominal surgery. Eighty-five percent of our sample reported that pain and/or fatigue impacted on their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of surgery.

The psychological measures did not prove to be strong predictors of postoperative pain, time of return to normal activity level or analgesic usage. The most powerful predictor of return to normal activity was the total amount of pain experienced, as measured by the McGill Pain Questionnaire, during the 7 day post-operative period.

Key words: Pain; Tubal ligation; Sterilization; Day-care surgery

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Economic and Clinical Outcomes of Microlaparoscopic and Standard Laparoscopic Sterilization

A Comparison

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Francisco A. R. Garcia, M.D., M.P.H., Ina Steinmetz, M.D., Bel Barker, M.D., and George R. Huggins, M.D.

OBJECTIVE: To compare microlaparoscopic surgical sterilization and standard laparoscopic sterilization with respect to cost effectiveness and patient preferences.

STUDY DESIGN: A retrospective study of all laparoscopic surgical sterilizations performed under general anesthesia at Johns Hopkins Bayview Medical Center—16 microlaparoscopies and 34 standard laparoscopies. Cases selected for review were limited to patients undergoing surgical contraception and not requiring additional, concurrent procedures. Laparoscopic surgical sterilization was performed using a double-puncture technique with silicone band application. In each case either a standard, 10-mm laparoscope or a 2-mm microlaparoscope was used, and the procedure was performed under general anesthesia. Postoperative pain management was

achieved by nonsteroidal antiinflammatory drugs and/or narcotic analgesia. All cases were performed by residents

under faculty supervision. Medical records and hospital billing records were reviewed, and a standardized telephone interview was conducted to assess postoperative quality of life and patient satisfaction.

A statistically greater number of subjects in the microlaparoscopic group reported overall satisfaction....

RESULTS: Both techniques were comparable in cost effectiveness. There was no significant difference in operating room time, average operating room costs, average ancillary department costs, instrument and supply costs, or length of stay. Postoperative discomfort was significantly less with microlaparoscopy ($P = .05$), and patient satisfaction was higher in the microlaparoscopy group.

CONCLUSION: Microlaparoscopy and the standard laparoscopic approach for surgical sterilization are asso-

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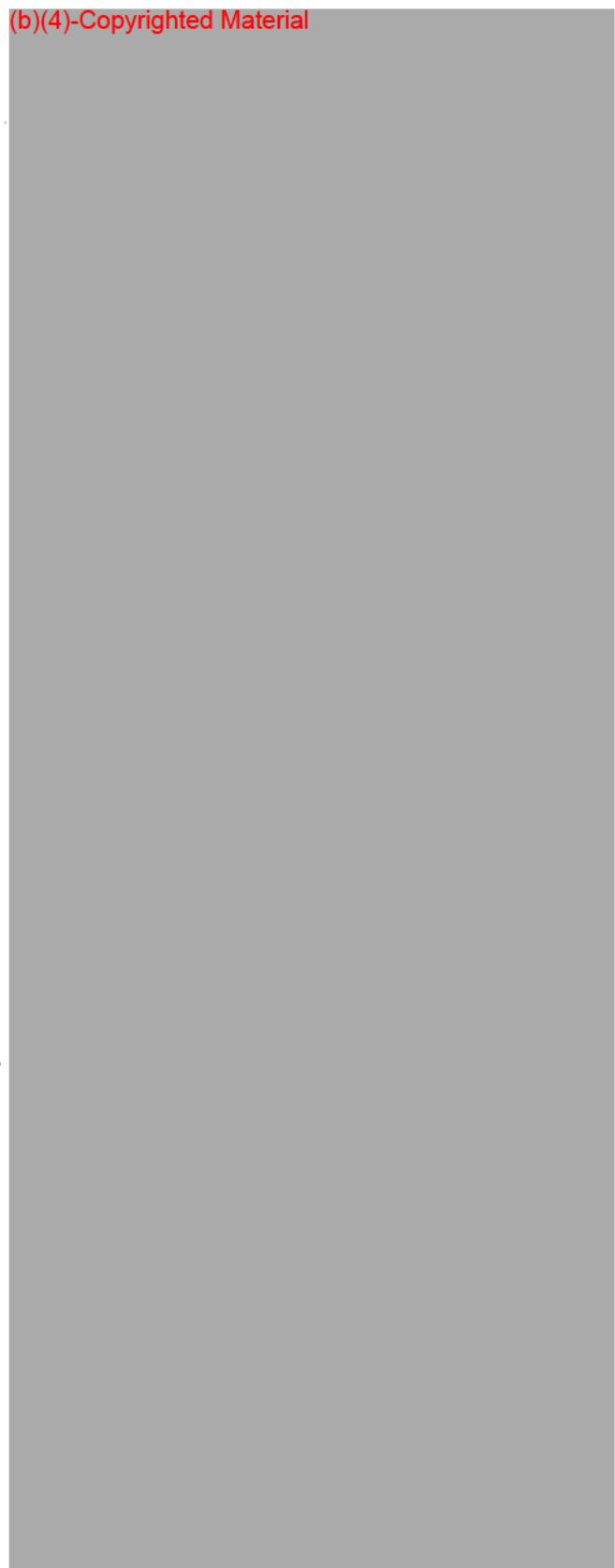
ciated with similar hospital charges. Postoperative pain and overall patient satisfaction were significantly better with microlaparoscopy than standard laparoscopy. (J Reprod Med 2000;45:372-376)

Keywords: laparoscopic surgical procedures; sterilization, tubal; minilaparoscopy.

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GLOBAL HEALTH OPTIONS

BIRTH CONTROL AND UNINTENDED PREGNANCIES

- This section explores the relationship between **Birth Control** and **Unintended Pregnancies** in the USA

INTRODUCTION - DATA

- Approximately 5.38 million pregnancies occur in the USA each year.
- Almost half (49% or ~2.65 million) of these are unintended pregnancies.
- Of the unintended pregnancies 46% (~1.2million) result in births and 54% (~1.4million) end in abortion.
- Teenagers (ages 15 -18) have the highest rate of unintended pregnancies.
- Surprisingly, the second highest rate is found in women aged 40 - 44 years.
- Only 40% of unintended pregnancies occur in women who do not use any form of birth control.
- The majority, 60%, occur in women using some form of birth control. This translates into approximately 1.4 million unintended pregnancies occurring in women using birth control at the time that they become pregnant.
- It is estimated that about 1 million unintended pregnancies happen because of improper use of Oral Contraceptives (Birth Control Pills).

DISCUSSION

- The rate of unintended pregnancies in the USA is quite high in comparison to the other developed nations of the world.
- The overall rate of unintended pregnancies has declined little over the past several decades.
- Given the above facts, it may be argued that unintended pregnancy represents an important public health concern in the USA.
- There are many risks and consequences associated with an unintended pregnancy; while abortion and negative socioeconomic issues are usually the predominant focus, the mortality and morbidity associated with a pregnancy in this context are very important and frequently overlooked.
- For example, consider the following. Childbirth is the most common reason for hospitalization in the USA and hospitalizations for pregnancy complications occurring before delivery account for more than 2 million hospital days per year, at a cost of greater than \$1 billion annually.
- For the overwhelming majority of women, effective contraception is much safer than childbirth.
- In 1995, 17.6 million women visited their health care providers to receive services for a Birth Control method. However, studies have found that women reported using some form of Birth Control during the month of conception for more than half (53%) of all unintended pregnancies.
- In this population of women, unintended pregnancy results from inconsistent or improper use of Birth Control, often Oral Contraceptives (Birth Control Pills).
- Women point to several reasons for inconsistent or improper use of Oral Contraceptives (Birth Control Pills). The major ones are : difficulties associated with remembering to take a pill every day, tolerability issues, especially breakthrough bleeding, and fears about the potential risks of Oral Contraceptive (Birth Control Pill) use.

CONCLUSION

- There is a very high number of unintended pregnancies occurring in the USA each year.
- An unintended pregnancy can have long-lasting and potentially dangerous medical consequences.
- By contrast, a planned pregnancy can facilitate an optimal outcome for both mother and offspring. The benefits of planning a pregnancy extend not only to the psychosocial and economical aspects but, most importantly, to the health aspects.
- For example, planning a pregnancy allows for the treatment of any preexisting medical conditions and the prevention or treatment of any potentially harmful infections while at the same time allowing for proper immunization management of the mother-to-be.
- Millions of women become pregnant despite using a method of Birth Control at the time of conception.
- While there are many factors that can contribute to the aforementioned failure of contraceptive methods, a large number of women report incomplete or improper use of Birth Control due either to intolerance of or displeasure with the side-effects of the method, or to misperceptions about the potential risks of using a particular method of Birth Control.
- In conclusion, the prevention of unintended pregnancies represents an important health concern and a challenge for both the public and the medical profession, in particular.
- Steps that might be considered in reducing unintended pregnancies are :
 - 1) Better informing the public about this problem and its implications.
 - 2) Better educating patients in the correct use of the available methods of Birth Control and dispelling the misconceptions about them.
 - 3) And most importantly, making available to the public as wide an array of Birth Control options as possible and continuing research efforts.

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ABOUT US

MISSION

Global Health Options wants to expose a worldwide audience to health information and products. The goal is to empower people to live a healthier life, gain a better understanding of their body, and have an optimal experience in times of illness.

HISTORY

Global Health Options arose from a need to inform the public about the great divide that exists in the arena of Birth Control, particularly between the Americans and their European counterparts. According to Dr. Felicia Stewart, a Birth Control expert that served in the Clinton administration: '**Women and men in the United States don't know that they're being shortchanged.**'

The options for Birth Control methods are far greater in Europe vs. the USA. What is perhaps even more troubling then that is the fact that a lot of the Birth Control options available in Europe have been developed in the USA and, sometimes, even tested on American women. Thus, Global Health Options presents information and, occasionally, products to the public in an effort to educate and improve the health of all people, regardless of geographical boundaries.

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Abortion Patients in 1994-1995: Characteristics and Contraceptive Use

By Stanley K. Henshaw and Kathryn Kost

Results of a 1994-1995 national survey of 9,985 abortion patients reveal that women who live with a partner outside marriage or have no religious identification are 3.5-4.0 times as likely as women in the general population to have an abortion. Nonwhites, women aged 18-24, Hispanics, separated and never-married women, and those who have an annual income of less than \$15,000 or who are enrolled in Medicaid are 1.6-2.2 times as likely to do so; residents of metropolitan counties have a slightly elevated likelihood of abortion. When age is controlled, women who have had a live birth are more likely to have an abortion than are those who have never had children. Catholics are as likely as women in the general population to have an abortion, while Protestants are only 69% as likely and Evangelical or born-again Christians are only 39% as likely. Since 1987, the proportion of abortions obtained by Hispanic women and the abortion rate among Hispanics relative to that for other ethnic groups have increased. The proportion of abortion patients who had been using a contraceptive during the month they became pregnant rose from 51% in 1987 to 58%. Nonuse is most common among women with low education and income, blacks, Hispanics, unemployed women and those who want more children. The proportion of abortion patients whose pregnancy is attributable to condom failure has increased from 15% to 32%, while the proportions reporting the failure of other barrier methods and spermicides have decreased. (Family Planning Perspectives, 28:140-147 & 158, 1996)

Annual national data describing women having abortions in the United States cover only basic demographic characteristics--age, race, ethnicity, marital status, and prior births and abortions--as well as the procedure used for the abortion and the length of the pregnancy. This information is collected by most states, and it is compiled and published at the national and state levels by the Centers for Disease Control and Prevention (CDC). However, some states have no abortion reporting system, and the CDC reports understate the number of abortions performed. The Alan Guttmacher Institute (AGI) conducts periodic surveys of all abortion providers throughout the country and uses the results together with the CDC data to estimate the number of abortions nationwide and the abortion rate according to a variety of characteristics.¹

This article reports information from a 1994-1995 AGI survey detailing a broad range of characteristics of abortion patients--socioeconomic status, religious affiliation, residence, childbearing intention and contraceptive use prior to the pregnancy. The survey, part of a larger project to update contraceptive failure rates, obtained usable questionnaires from 9,985 respondents in a stratified national sample of 100 clinics, hospitals and physicians' offices in all regions of the country. This information updates the findings from a similar 1987 survey of 9,480 abortion patients in a stratified national sample of 103 facilities.²

Methodology

Data Collection

Data were collected by means of a self-administered questionnaire, available in both English and Spanish, which the staff of abortion facilities distributed to patients. The facilities decided when to present the questionnaire to patients; most gave it to women to complete along with other paperwork while they waited for the procedure. Attached to the questionnaire was an introduction explaining that the survey was voluntary, anonymous and for research only.

The questionnaire was a single sheet of paper with questions on both sides covering women's characteristics and prior contraceptive use. Because data from the 1995 National Survey of Family Growth (NSFG) were to be used in conjunction with findings from this survey to calculate contraceptive failure rates, the questions had been slightly revised since 1987, to replicate to the extent possible those used in the 1995 NSFG.

The facilities selected for the study were drawn from a list of all hospitals, clinics and physicians' offices where abortions are performed. The list, which had been updated in 1993 for AGI's periodic survey of abortion providers, was stratified by provider type (hospital or nonhospital facility) and by the number of abortions performed in 1992, rounded to the nearest 10 (30-390; 400-1,990; 2,000-4,990; or 5,000 or more). Facilities that reported fewer than 30 abortions were impractical to survey, but their exclusion would cause little bias, since they accounted for only 0.4% of all reported abortions in 1992.³

Within each stratum, facilities were listed by state, and states were arranged geographically within census region; for our analysis, we selected facilities at equal intervals on the list (such as every fifth or every seventh one), depending on the stratum. Each facility was asked to administer the questionnaire to every woman who obtained an abortion during a specified time period ranging from two to 12 weeks, depending on the facility's caseload. If a facility declined to participate or did not obtain usable questionnaires from at least half of the target women throughout the specified time, it was replaced by the next facility on the list, which in most cases was in the same or a neighboring state and in the same region.

We initially sampled 113 abortion providers--19 hospitals and 94 nonhospital facilities. Of these, 11 and 46, respectively, had to be replaced--31 facilities were unable or unwilling to participate, 11 had closed, 11 were unable to administer the survey for the required number of weeks or had a response rate of less than 50%, and four had caseloads that had fallen below 30 per year. (In some cases, the replacement facilities also had to be replaced.) Nine of the hospitals and 18 of the other facilities that had to be replaced performed 30-390 abortions a year. Since facilities of this size provide only 9% of all abortions, selection bias among them would have had only a small effect on the sample. We ultimately obtained usable data from 13 hospitals and 87 nonhospital facilities; the 13 facilities that could not be replaced were in the smallest caseload category.

Participating facilities were asked to report the number of abortions they performed during the specified time frame; the total came to 11,288. Usable questionnaires were obtained from 9,985 of the women, for a response rate of 88%. At our request, the providers supplied information about the age, race, ethnicity and Medicaid coverage of 562 nonrespondents; no information was available for the remaining 741 nonrespondents. Most nonresponse resulted

from women's refusal to participate, facilities' failure to distribute questionnaires or lack of time for the patient to complete the questionnaire. Of the usable responses, 87% were obtained during the second half of 1994 and 13% during the first half of 1995.

To correct for any bias produced by deviation from the original sampling plan and nonresponse, a three-stage weighting process was followed. First, individual weights were developed to adjust for the demographic characteristics of the 562 nonrespondents for whom the facilities provided data. Second, facility-level weights were used to adjust for the other 741 nonrespondents. Third, stratum weights were constructed to correct for departures from the number of facilities to be sampled in each grouping by caseload and provider type. With the final weight adjusted to a mean of 1.0, the standard deviation was 0.22 and the range was 0.54-3.27.

The rate of nonresponse on individual items was generally 2-4%, but ranged from less than 2% on Medicaid coverage to 20% on household income. Instead of assuming that the nonrespondents were similar to all those who had answered a question, we imputed missing information on the basis of the responses of other women with similar characteristics, using a "hot-deck" procedure.*

For a sample of 9,985, the 5% confidence interval is $\pm 1\%$ for a proportion of 50%, and less for proportions other than 50%. Because the sample was clustered and weighted, we have used the 3% significance level, for which the confidence interval is $\pm 1.1\%$ or less. All of the differences noted in this article are significant at the 3% level. Since nonrandom error is always a possibility in survey research, however, one should be cautious in drawing conclusions from small differences.

Representativeness of the Survey

As a check on the representativeness of the survey, we compared the results with the adjusted CDC compilations of state reports for 1991,⁴ the latest year for which detailed statistics have been published. **Of the characteristics on which comparisons were possible (age, race, ethnicity, marital status, parity and number of prior abortions), the results were within two percentage points of each other for all subgroups except "other" race (not white or black) and Hispanic ethnicity.

In our survey, 8% of abortion patients reported their race to be Asian, Pacific Islander, American Indian or Alaskan native; in the adjusted CDC statistics, by comparison, the proportion in these racial groups is 4%. There are three possible reasons for the discrepancy: First, the 1991 CDC statistics include no data on abortion patients' characteristics for California, which has a large Asian population. Second, in the AGI survey, 12% of those who reported their ethnicity as Hispanic, a relatively large proportion, reported their race as American Indian or Asian; clinic staff who complete state abortion reporting forms probably tend to record Hispanics as white or black. Excluding Hispanic women, 5% of respondents in the AGI survey were of races other than white or black. Third, the proportion of Asians in the U.S. population grew between 1991 and 1994-1995.

An even larger percentage-point difference emerged in the proportion of women reported to be Hispanic: 20% in the survey and 13% in the adjusted CDC statistics. One possible explanation for this difference is that the survey may have sampled facilities that happened to have a large proportion of Hispanic patients. Since Hispanic patients tend to be concentrated

in certain clinics and in certain states, the survey design produces a higher standard error for this characteristic than for variables that are more uniformly distributed among facilities.

Two other factors, however, could have caused the state statistics compiled by the CDC to underestimate the proportion of Hispanics among women having abortions. First, as noted, characteristics are not known for abortion patients in California, which has both a high abortion rate and a high proportion of Hispanics. Second, CDC reports have indicated that sharp increases have occurred in the proportion of abortions obtained by Hispanic women: 10% in 1990, 14% in 1991 and 15% in 1992.⁵ While this rate of increase is unlikely to continue, the Hispanic proportion may well have been higher in 1994-1995 than it was in 1991.

Overall, the comparison with adjusted CDC data offers reassurance that the survey accurately represents the universe of women having abortions. Even if the survey represented the universe perfectly, some differences between the two data sources would be likely because the 1991 CDC data are based on only 45-55% of all abortions, depending on the characteristic, and on only 33% of abortions among Hispanic women. In addition, changes may have occurred between 1991 and 1994-1995.

Abortion Indices

We were unable to calculate the abortion rate (the number of abortions per 1,000 women) for each subgroup because the total number of abortions performed in 1994 or 1995 is unknown. Instead, we have created an abortion index that allows subgroups to be compared in the same way they could be if their rates were known.

The index is equivalent to the ratio of the abortion rate for each subgroup to the overall abortion rate. It is calculated by dividing the proportion of abortion patients in a subgroup by the proportion of U.S. women 15-44 in that subgroup. *** An index value of 1.0 would indicate that a subgroup's abortion rate was the same as the rate for all women 15-44; values under 1.0 indicate rates below the rate for all women, while values exceeding 1.0 represent above-average rates. The index may be thought of as the "relative abortion rate," since it is the abortion rate of a subgroup relative to that of all women.

Since age is strongly associated with the abortion rate, differences between subgroups may result partly from differences in the ages of women in the subgroups. Therefore, to estimate what the index would be if the age distribution of each subgroup were the same as the age distribution of all women 15-44, we also calculated age-standardized indices for 1994-1995 and for 1987. The age-standardized index for 1987 was derived from the 1987 AGI survey.⁶

Women's Characteristics

Table 1 shows the percentage distribution of women who had abortions and of all women aged 15-44, according to the characteristics about which the survey solicited information. As the table indicates, women aged 20-24 obtain 33% of abortions, and teenagers obtain 22%. Women aged 15-17, with an index of 1.0, are as likely as all women aged 15-44 to have abortions, and those aged 18-19 and 20-24 are about twice as likely to do so (indices of 2.0 and 2.2, respectively). Abortion rates decline sharply in the older age-groups; the likelihood of abortion among women aged 30 and older is no more than 77% of that among all women.
< TD>

< TD>1.23
 < TD>66.2
 < TD>34.4
 < TD>
 < TD>
 < TD>79.6

Table 1. Percentage distribution of U.S. abortion patients, and of all women aged 15-44 and age-standardized index, 1994-1995 and 1987; all by selected characteristics

Characteristic	% distribution		Abortion			Age-standardized			Characteristic	% dist
	Abortion patients	Women 15-44Y	index,		1987	index		Ab-		
			1994-1995	1994-1995		1987	pat			
Age-group								Religion§§ (cont.)		
<15	1.2	u	na	na	na		White non-Hispanic			
15-17	8.8	8.8	1.01	na	1.15y		Protestant	1		
18-19	11.5	5.7	2.01	na	2.23y		Catholic	1		
20-24	32.8	15.2	2.16	na	1.95y		All others	6		
25-29	21.4	16.1	1.33	na	1.18y					
30-34	14.4	18.8	0.77	na	0.64y		Born-again/Evangelical			
35-39	7.5	18.6	0.40	na	0.35y		Yes	1		
>=40	2.3	16.8	0.14	na	0.12y		No	8		
Race							Education			
White	61.3	81.2	0.76	0.76	0.83		3/8th grade	4		
Black	31.1	14.0	2.23	2.12	1.99		9th-11th grade	1		
Other	7.6	4.9	1.56	1.55	1.07§		H.S. graduate or GED	3		
							Some college or			
Ethnicity							associate's degree	3		
Hispanic	20.2	10.6	1.90	1.75	1.44		College graduate	1		
Non-Hispanic	79.8	89.4	0.89	0.90	0.96					
							Enrolled in school			
Marital							Yes	3		

status							
Married	18.4	49.9	0.37	0.57	0.52	No	6
Separated	7.2	3.3	2.17	2.83	2.62		
Divorced	9.4	8.6	1.09	1.47	2.05	Currently employed	
Widowed	0.5	0.7	0.78	1.97	2.01	Yes	
Never-married	64.4	37.5	1.72	1.34	1.35	No	3
Cohabiting						Family income	
Yes	20.2	5.8	3.47	3.06	4.65	<\$15,000	2
No/married	79.8	94.2	0.85	0.86	0.86	\$15,000-\$29,999	1
						\$30,000-\$59,999	3
No. of live births						>=\$60,000	1
0	45.4	41.2	1.10	0.78	0.92		
1	24.7	18.2	1.36	1.30	1.21	Has Medicaid coverage	
2	17.8	23.8	0.75	1.25	1.03	Yes	2
3	7.7	11.1	0.69	1.17	1.14	No	7
>=4	4.4	5.8	0.76	1.48	1.73		
						Intends more children	
Religion§§						Yes	6
Protestant	37.4	53.9	0.69	0.73	0.74	No	3
Catholic	31.3	30.9	1.01	0.97	0.95		
Jewish	1.3	1.2	1.08	1.03	0.69	Region of residence	
Other	6.3	8.1	0.78	0.77	2.04	Metropolitan	8
None	23.7	5.9	4.02	3.87	3.68	Nonmetropolitan	1
Total	100.0	100.0	1.00	1.00	1.00	Total	1

YData for 1994 except Medicaid status (1993), religion (1993-1995) and childbearing intent
 yNot age-standardized. §Not exactly comparable to 1994 because all Hispanics were classified
 44. yStandardized on women 20-44. §§Based on women 18-44. YIncome breaks for 1987
 Notes: In this and subsequent tables, na=not applicable; u=unavailable. Sources: POPULA
 F.W. Hollmann and P. Montgomery, "U.S. Population Estimates, by Age, Sex, Race, and Hi
 Projections Branch, U.S. Bureau of the Census, Washington, D.C., 1995. Marital and coha
 Status and Living Arrangements: March 1994," Current Population Reports, Series P-20, N
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tabulations of data from five Gallup polls, Roper Center for Public Opinion Research, Storrs
employment status and income--U.S. Bureau of the Census, Current Population Survey, un
tabulation of the March 1994 Current Population Survey. **Childbearing intentions**--special
Growth. **Metropolitan status**--U.S. Bureau of the Census, *1990 Census of Population, Was*
Population Division, U.S. Bureau of the Census, "Resident Population and Change for Metr
July 1, 1994," PPL -27, Washington, D.C., 1995. **1987 DATA:** See reference 2.

Teenagers' relative abortion rate has declined since 1987, when the index was 1.2 for 15-17-year-olds and 2.2 for 18-19-year olds. The relative abortion rate increased among women in their 20s, and the highest rate now occurs among women aged 20 -24, rather than among 18-19-year-olds.

Although white women obtain 61% of abortions, their abortion rate, reflected by an index of 0.8, is well below that of women of other races. The index for black women is 2.2, or nearly triple that of white women, and the differential has increased since 1987. The index for women of races other than black or white is 1.6, but this may be inflated by the inclusion of some Hispanic women in this group (as explained in the methodology section). In the 1987 survey, which classified all Hispanic women as white or black, the age-standardized abortion rate for women of "other" races was only slightly above that of all women (1.1); the 1994-1995 index would be about the same as the 1987 rate if Hispanics were excluded from this group.

Hispanic women have a much higher abortion rate than non-Hispanics, but their rate is not as high as that of black women. The index for Hispanics is reduced somewhat when standardized for age (from 1.9 to 1.8), but is still roughly twice that of non-Hispanic women (0.9). The age-standardized index for Hispanics has increased substantially from its 1987 level of 1.4.

As they have in the past, never-married women obtain the bulk of abortions (64%); married women account for only 18% of procedures. The age-standardized abortion rate for married women is slightly more than half the rate for all women. The rate is highest among separated women--almost three times the overall rate. Since 1987, the relative rate has decreased among divorced women.

Women living with a partner to whom they are not married account for 20% of the abortion sample, but only about 6% of women in the population; their probability of having an abortion is 4.1 times that of women who are not cohabitating, or 3.6 times after adjustment for age. The differential appears to have decreased since 1987, when the age-standardized indices suggested that cohabiting women were 5.1 as likely as others to have an abortion. However, the decline may be partly due to random error in the measurement of cohabitation in the general population.

Some 55% of women having abortions in 1994-1995 have had at least one live birth. When age is taken into account, women who have had a child are substantially more likely than others to have an abortion (index values of 1.2-1.5 vs. 0.8). As in 1987, the highest age-standardized index is found among women who have had four or more births. In all, 72% of abortion patients who have given birth are unmarried, and 48% of unmarried abortion patients have borne children (not shown).

For 55% of respondents, this abortion was their first; 7% had had three or more abortions (not shown). In 1987, 57% had not had an abortion before, and 5% had had at least three. The principal reason for the continuing long-term increase in the proportion of abortion patients who have had prior abortions is that with each year since the procedure was legalized, a larger proportion of women in the population have had a first abortion.⁷ The proportion of abortion patients who have had a previous abortion reaches 60% among women 30 and older, who have had more years of exposure to the risk of a first abortion than have younger women.

Protestants account for 37% of abortion patients, but for 54% of the general population of women 18-44, as measured in five 1993-1995 Gallup polls combined;⁸ the resulting age-standardized index is 0.7. The age-standardized abortion rates for Jewish and Catholic women are close to the rate for all women. Women who claim no religious identification appear to have abortions at about four times the rate of women who name a religion.**** None of these rates have changed noticeably since 1987 except the rate for Jewish women, which is unstable because the sample of Jewish women in the Gallup polls and the proportion of the population who are Jewish are small. Among women of "other" religions, the index is 0.8 for 1994-1995, down from 2.0 for 1987. The apparent change may be attributable to differences in the data used for the national comparison: The proportion of women who named a religion classified as "other" was only 2% in the 1982 NSFG, which was used for the 1987 comparisons, but was 8% in the 1993-1995 Gallup polls.

To further explore the difference between the abortion rates of Protestants and Catholics, we calculated the indices after excluding nonwhites and Hispanics, who have high abortion rates. As expected, this exclusion reduced the abortion rate of both Protestants and Catholics, but the difference between the religious groups changed little; the age-standardized rate for Catholic women is 29% higher than that for Protestants (0.6 vs. 0.5). The same pattern was found in 1987.

The questionnaire asked whether the respondent considered herself a "born-again Christian or Evangelical Christian"; this question was taken from a Gallup poll so that comparative data would be available. The proportion responding affirmatively represented a slight increase from 1987 (18% vs. 16%). According to the Gallup polls, 46% of all women 18-44 consider themselves born-again or Evangelical Christians,†so the abortion rate among this group is much below the rate for other women (indices of 0.4 and 1.5, respectively).

The distribution of abortion patients by educational attainment is similar to that of women in the population, with the difference that women with some college but not a bachelor's degree are overrepresented among abortion patients, while college graduates are slightly underrepresented. The age-standardized index, which includes only women aged 20-44, also shows women with some college education to be slightly more likely than others to have an abortion. Among abortion patients aged 20 and older, 57% have attended college or have some postsecondary education.

Women's distribution by level of education as found in the survey differs markedly from the distributions reported by state health departments and published by the National Center for Health Statistics (NCHS). In 1988, the most recent year for which NCHS data are available, 54% of women having abortions in an 11-state area had a high school diploma but no further schooling;⁹ in our survey, the proportion with this level of education was 30%. The NCHS reported about the same proportion of college graduates as our survey (35%), while the

proportions in other categories were lower. If the NCHS reports are accurate, women who completed their education with a high school diploma have a much higher abortion rate than women of any other educational level.

A higher proportion of abortion patients than of all women 15-44 are enrolled in school (30% vs. 25%). When age is adjusted for and women younger than 20 are omitted, enrolled women are 15% more likely to have an abortion than are women not enrolled in school. Among teenagers, the relationship is reversed (not shown): For those aged 15-17, the abortion index is 5.0 among women who have left school and 0.7 among enrolled women; for 18-19-year-olds, the index values are 2.4 and 1.9, respectively. The abortion index for women aged 20 and older who are in school fell from 1.5 to 1.1 between 1987 and 1994-1995.

Although in 1987 employed women had a higher abortion rate than those not working, this was no longer the case in 1994-1995. In the latest survey, 66% of abortion patients were employed, the same proportion as among women in the population.

Women from families with an annual income of less than \$15,000 have a higher abortion rate than do women from families with an income of \$15,000-\$59,999 (indices of 1.9 and 0.9-1.1, respectively), while those with a family income of \$60,000 or more have a lower rate (0.5). Age standardization reduces the income differentials somewhat, but the probability of having an abortion is still three times as high for the lowest income group as for the highest.

The high relative abortion rate of low-income women is reflected in the rate according to Medicaid coverage. Twenty-seven percent of patients say they are covered by Medicaid (although not necessarily for abortion, since only 13 states and the District of Columbia allowed Medicaid to pay for abortion services in 1995), compared with 13% of all U.S. women of reproductive age. The age-standardized indices reveal that women with Medicaid coverage are twice as likely as others to have abortions (1.7 vs. 0.9). The differential is lower than in 1987, when women with Medicaid coverage were nearly three times as likely as others to have abortions.

Some of the differential by Medicaid coverage may be spurious, since most of the states that fund abortions under Medicaid extend eligibility to some low-income pregnant women who would not otherwise qualify, while in the population statistics, such women are not counted as being covered by Medicaid. It is unclear how many women who are not already Medicaid recipients are able to obtain Medicaid coverage for an abortion, but the number may be low.

Women covered by Medicaid have a number of characteristics that may contribute to their relatively high abortion index: They are disproportionately nonwhite, unmarried and poor, all characteristics associated with high abortion rates. And many Medicaid-eligible women are covered by that program because of a prior unplanned pregnancy they carried to term, evidence of difficulty in preventing pregnancy.‡

A prior study found that Medicaid funding of abortion made abortion services accessible to women who would otherwise have carried unintended pregnancies to term.¹⁰ We find that in states where Medicaid pays for abortions, women covered by Medicaid have an abortion rate 3.9 times that of women who are not covered, while in states that do not permit Medicaid funding for abortions, Medicaid recipients are 1.6 times as likely as nonrecipients to have abortions. Although the difference may result partly from the ability of some women seeking abortions to qualify for Medicaid because they are pregnant, the magnitude of the difference

indicates that Medicaid coverage of abortion has an important effect on the ability of poor women to end unwanted pregnancies.

Sixty-six percent of abortion patients intend to have children (including 1% who are unsure). This proportion is lower than that in 1987 (70%), probably because of the older age distribution of the population and of women having abortions. It is higher than the proportion of all women aged 15-44 who intend to have more children (48%), however, reflecting the relatively young age of abortion patients. The age-standardized indices suggest that women who intend to have no more children are 9% more likely to have abortions than are women who intend more children.

As expected, a large majority (89%) of women having abortions live in counties classified by the federal government as metropolitan, and metropolitan women are twice as likely as nonmetropolitan women to have abortions (indices of 1.1 and 0.6, respectively). The comparatively low abortion index of nonmetropolitan women may reflect their difficulty in gaining access to abortion services, which are unavailable in the counties where 85% of nonmetropolitan women reside.¹¹ The limited availability of abortion facilities is indicated by the finding that 43% of the patients surveyed traveled outside their home county for abortion services (not shown). In 1987, by contrast, 39% of abortions took place outside the woman's county of residence.

Contraceptive Use

The patterns of contraceptive use among abortion patients may or may not mirror the use patterns of all women at risk of unintended pregnancy. Each contraceptive method entails a different probability of becoming pregnant, and women's method choice often differs by their socioeconomic and demographic characteristics. Consequently, users of each method may differ in their likelihood of carrying an unexpected pregnancy to term or of having an abortion. For example, women who use only periodic abstinence may, for religious or other reasons, be more likely than users of other methods to carry an unexpected pregnancy to term.

Patterns of contraceptive use among abortion patients therefore result from the combined effect of three factors: the patterns of use among all women, use-failure rates and the likelihood that a woman with an unplanned pregnancy will have an abortion. Changes in the patterns of prior contraceptive use of abortion patients over time can result from changes in any or all of these factors.

Use Status at Conception

Respondents were asked what contraceptive, if any, they had last used before they became pregnant, when they had stopped using that method and how long they had used it. They were considered to have had a contraceptive failure if they were using the method during the month of their last menstrual period. They also were counted as having had a contraceptive failure if they said they had stopped using the method during the month of their last menstrual period, but in response to another question they said they had not stopped using all methods before becoming pregnant. This definition of contraceptive failure, conventionally referred to as "use-failure," means the woman considered herself a method user during the month she became pregnant, although she may not have used a method consistently or correctly.¹²

Overall, 58% of women having abortions have experienced a contraceptive failure; 31% have used a method in the past but were not using one during the month in which they conceived, and 11% have never used any method (Table 2). Even among women younger than 18, 55% were using a method, almost the same proportion as among women 20 and older (57-59%).

Table 2. Percentage distribution of abortion patients, by contraceptive use status during the month in which they became pregnant, according to year and selected characteristics				
Survey year and characteristic	Current user	Prior user	Never-user	Total
1994-1995	57.5	31.2	11.2	100.0
Age-group				
<18	55.4	25.3	19.3	100.0
18-19	58.6	29.1	12.4	100.0
20-29	57.1	33.3	9.7	100.0
>=30	59.0	30.1	10.8	100.0
Poverty status^Y				
0-99%	49.0	34.3	16.7	100.0
100-149%	53.2	33.5	13.3	100.0
150-199%	58.2	31.1	10.7	100.0
>=200%	63.5	28.9	7.6	100.0
Race/ethnicity				
White ^Y	67.0	27.2	5.8	100.0
Black ^Y	52.0	36.1	11.9	100.0
Hispanic	44.7	34.3	21.0	100.0
Other	54.2	28.6	17.1	100.0
1987	51.3	39.7	9.0	100.0
Age-group				
<18	39.4	33.9	26.7	100.0
18-19	48.8	39.8	11.4	100.0
20-29	51.9	41.9	6.2	100.0

>=30	58.8	36.6	4.6	100.0
Poverty status^Y				
0-99%	43.0	44.2	12.7	100.0
100-149%	48.9	43.0	8.0	100.0
150-199%	52.5	40.2	7.3	100.0
>=200%	57.1	35.6	7.4	100.0
Race/ethnicity				
White	57.6	36.1	6.2	100.0
Black	41.8	47.7	10.5	100.0
Hispanic	42.1	41.2	16.7	100.0
Other	53.7	31.9	14.4	100.0
^Y Poverty status is the woman's annual family income expressed as a proportion of the federally designated poverty level for the year in which she was interviewed. The designated level was \$12,320 for a family of four in 1994 and \$ 12,590 for a family of four in 1995. ^y Excluding Hispanics. <i>Source: 1987 data--See reference 2.</i>				

According to the 1988 NSFG, 90% of women at risk of unintended pregnancy are using a contraceptive method and 10% are not.¹³ The abortion indices for current users and nonusers are therefore 0.6 and 4.3, respectively, indicating that women using any method are only about 15% as likely to have an abortion as are women using no method. In other words, even though contraceptive use is often imperfect, it reduces the probability of having an abortion by about 85%.

Poverty status is strongly associated with contraceptive use; 64% of the women whose family income is at least twice the federal poverty level were using a method, compared with 49% of those with an income under the poverty level. Of the racial and ethnic groups, white non-Hispanic women are the most likely to have been using a method (67%), while Hispanic women are the least likely (45%).

The proportion of abortions resulting from contraceptive failure (58%) represents an increase of 12% from 51% in 1987. The increase occurred entirely among women younger than 30 and was greatest among teenagers. While contraceptive use differed sharply by age in 1987, these differences had almost disappeared by 1994-1995. The increase in use occurred equally among all poverty-status groups and among white and black women. Little change occurred, however, among Hispanics and women of races other than white and black.

Both educational attainment and employment status were positively associated with contraceptive use at the time of conception among abortion patients in 1987 and in 1994-1995 (not shown). Of the religious groups, Protestants are the most likely to have been using

a method (60%), while Catholics are the least likely (56%). Among women who became pregnant while using a method, 56% had been using the method for 12 months or less.

Prior Use

Of the 42% of women who were not using a method when they became pregnant, 74% (or 31% of the entire sample) had used one at some time. The majority of prior contraceptive users had most recently relied on either the pill (55%) or the condom (29%). This represents an important shift since 1987, when 74% of prior users had taken the pill and 22% had used the condom.

The women surveyed in 1994-1995 had become pregnant within a fairly short time after discontinuing method use: 32% within the first month and 59% within three months. Among those surveyed in 1987, only 18% had become pregnant within the first month. Additionally, prior users of the pill or the condom seem to have become pregnant more quickly after stopping use than had their counterparts in 1987. In 1994-1995, 53% of prior pill users and 76% of prior condom users became pregnant within three months of stopping use; by comparison, the proportions in 1987 were 44% and 69%, respectively (not shown).

Never-Use

As might be expected, the proportion of abortion patients who have never used any contraceptive method is highest among women younger than 18 (19%); only 10-11% of those aged 20 and older have never used a method. And abortion patients in the two lowest income groups are far more likely to have never used a contraceptive method than are those in higher income groups (13-17% vs. 8-11%).

The proportion who are never-users declines from 21% of Hispanics and 17% of those of races other than white and black to 12% among blacks and 6% among whites. The relatively high proportion of never-users among Hispanic women and those of other races may reflect a concentration of immigrants from cultures where contraceptive prevalence is lower than in the United States. For example, 26% of women who completed the questionnaire in Spanish (presumably the most recent immigrants) had never used a method, compared with 18% of Hispanics who preferred the English version of the questionnaire. Only 8% of Protestants have never used a method, compared with 13% of Catholics (not shown).

Between 1987 and 1994-1995, the proportion of never-users declined markedly among women younger than 18, but increased among women aged 20 and older. Women who completed the questionnaire in Spanish were much older, on average, than other women (only 8% were teenagers, compared with 23% of women who completed the questionnaire in English); these women may in part account for the increase in the proportion of older women who have never used a method. The proportion of women who have never used a contraceptive also increased among the lowest income group (from 13% to 17%) and among those at 100-149% of the poverty level (from 8% to 13%).

Multivariate Analyses

Many of the observed subgroup differences in contraceptive use may reflect confounding of the abortion patients' demographic and socioeconomic characteristics. For example, racial and ethnic differences in the proportion of abortion patients who were using a method when

they became pregnant may reflect different poverty-status distributions among racial and ethnic groups. We therefore constructed logistic regression models to identify the variables most strongly associated with having been a method user at conception and with never having used any method.

Table 3 (page 146) shows that with other variables controlled, women aged 20 and older are considerably less likely than those younger than 18 to have used a contraceptive at the time of conception (odds ratios of 0.6). The 1988 NSFG found that among women at risk of unintended pregnancy, teenagers were slightly less likely than older women to be using a contraceptive.¹⁴ Since teenagers tend to use less effective methods than older women,¹⁵ teenagers who were using a method are overrepresented among abortion patients.

Table 3. Odds ratios describing the association of abortion patients' characteristics with contraceptive use during the month of conception and with never-use of contraceptives		
Characteristic	Used	Never used
Age-group		
<18	1.000	1.000
18-19	0.797	0.776
20-29	0.618*	0.747*
>=30	0.605*	0.968
Race/ethnicity		
White or other	1.000	1.000
Black	0.606*	1.560*
Hispanic	0.559*	2.230*
Poverty status		
<100%	1.000	1.000
100-149%	1.140	0.829
150-199%	1.227*	0.647*
>=200%	1.328*	0.571*
Marital status		
Never-married	1.000	1.000
Married	1.093	0.811
Formerly married	0.960	0.892

Education		
<H.S.	1.000	1.000
H.S. graduate	1.323*	0.748*
Some college	1.890*	0.416*
>=college	2.179*	0.415*
Religion		
Protestant	1.000	1.000
Catholic	0.957	1.397*
Jewish	0.787	0.700
Other/none	0.983	1.422*
Employed		
Yes	1.000	1.000
No	0.864*	1.371*
Intends more children		
Yes	1.000	1.000
No	1.181*	0.906
*p<.03. A significance level of .03 was chosen as a more conservative test than .05 to allow for possible increased variance due to clustering, weighting and imputation of data.		

Compared with white women and those of other races, blacks and Hispanics are less likely to have used a method (odds ratio of 0.6 for each). Higher economic status, more education, being employed and not wanting more children are positively associated with contraceptive use during the month the conception occurred.

Women aged 20-29 are significantly less likely than the youngest women to have never used a method (odds ratio of 0.7). Blacks and Hispanics are more likely than other women to have never used a method (1.6 and 2.2, respectively); of the variables included, Hispanic origin is most strongly associated with lack of contraceptive experience. The odds that a woman has never used contraceptives decrease as income and educational attainment increase. Catholics and women without a religious identification (or followers of "other" religions) are more likely than Protestants never to have used contraceptives (odds ratio of 1.4 in each case). Women who are not employed in a paid job are more likely never to have used contraceptives than those who are employed (1.4).

Method Used at Conception

Table 4 shows that among abortion patients who were using a method during the month they became pregnant, the condom was the method most commonly used. (The table lists the methods in decreasing order of effectiveness. Women who reported use of more than one method are assigned only to the most effective one; for example, a woman who reported use of both the pill and the condom would be classified as having used the pill.) Of all abortion patients surveyed in 1994-1995, 32% had been using the condom, 12% the pill, 6% withdrawal, 2% periodic abstinence and 1% or fewer each of the other methods. (Written-in responses indicated that some of the pregnancies categorized as injectable failures occurred among women who had intended to continue using the method but were unable to obtain the injection by the required date.)

Table 4. Percentage distribution of abortion patients by contraceptive method used at time of conception, according to year		
Method	1994-1995	1987
Sterilization	0.2	0.2
Implant	0.1	na
IUD	0.1	0.3
Injectable	0.5	na
Pill	11.7	13.3
Condom	32.4	14.8
Female condom	0.2	na
Diaphragm	1.1	5.2
Sponge	1.0	4.7
Foam	0.9	2.0
Suppository	0.9	1.3
Periodic abstinence	2.3	3.8
Withdrawal	5.9	5.7
Other	0.2	0.1
None	42.5	48.7
Total	100.0	100.0

Source: 1987 data--unpublished tabulations from the 1987 abortion patient survey (see reference 2).

The distribution of women by method use in 1994-1995 is sharply different from that in 1987, when only 15% had been using the condom. While reliance on the condom increased

among abortion patients, use of almost all other methods decreased; the diaphragm and sponge saw particularly sharp declines (from 5% to 1%).

To check whether the increase in condom use reflects greater use of condoms at the same time as another method (such as a spermicide), we tabulated the number of respondents who indicated that they had used multiple methods. Among condom users, 46% also checked another method in 1987, compared with only 31% in 1994-1995. Thus, the results suggest a switch to condom use rather than the use of condoms in addition to other methods. Of course, this may not accurately reflect trends in multiple use in the population generally, since women who used the condom together with another method to avoid infection with the human immunodeficiency virus or other sexually transmitted diseases would be less likely to experience an unintended pregnancy and abortion.

Among the women who experienced contraceptive failure, the methods used differ little among the racial or ethnic groups (Table 5). The largest differences are that black women are more likely than nonblack and Hispanic women to have used the condom and less likely to have used withdrawal. Age differences are marked: Whereas 76% of women younger than 18 had used condoms, only 49% of women 30 or older had used this method. Pill use peaked (at 25%) among women aged 20-29, while use of "other" methods (mainly the diaphragm, sponge, spermicides and periodic abstinence) increased sharply with age, from 1% of women younger than 18 to 24% of those 30 and older. Possibly because age is correlated with income, the proportion who used other methods also increased as family income as a proportion of the poverty level rose. Otherwise, there is little association of method used with poverty status.

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Table 5. Percentage distribution of abortion patients who were using a contraceptive according to selected characteristics

Year and method	Total	Race/ethnicity			Age-group			
		White/other	Black	Hispanic	<18	18-19	20-29	>=30
1994-1995								
Long-acting	1.5	1.2	1.5	2.2	0.3	1.3	1.5	2.0
Pill	20.3	19.0	21.6	23.0	11.0	16.2	24.8	16.1
Condom	56.6	55.5	61.2	53.2	76.0	64.6	54.9	48.9
Withdrawal	10.3	12.1	6.1	10.5	11.3	14.5	9.7	9.2
Other	11.3	12.1	9.6	11.0	1.4	3.4	9.0	23.7

1987								
Long-acting	1.0	0.8	0.8	2.1	0.0	0.0	0.8	2.5
Pill	26.0	20.9	39.5	30.9	18.3	29.1	31.2	14.0
Condom	28.7	31.4	23.1	22.7	47.4	34.3	25.2	26.8
Withdrawal	11.1	12.0	7.6	12.4	29.4	20.4	8.8	4.1
Other	33.2	34.9	29.0	31.9	5.0	16.2	34.1	52.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Excluding Hispanics. Sterilization, implant, injectable and IUD. *Source: 1987 data--unpublished survey (see reference 2).*

Between 1987 and 1994-1995, condom use among abortion patients who were using a method when they became pregnant increased dramatically among all women, regardless of race, ethnicity, age or poverty status; the increase was greatest among black and Hispanic women. In the same time period, pill use declined among abortion patients who had a contraceptive failure. This decline occurred primarily among blacks and Hispanics, but substantial decreases also took place among women of all ages except those 30 and older, and among those of all income levels except the highest.

The dramatic increase in condom use among teenage abortion patients was accompanied by a large decrease in the proportion using withdrawal. Among those younger than 18, 29% had been using withdrawal and 47% had been using the condom in 1987, while in 1994-1995, only 11% were using withdrawal and 76% relied on condoms. Among women 20 and older, the increase in condom use coincided with a drop of 25 percentage points or more in the use of "other" methods.

Discussion

The risk of unintended pregnancy leading to abortion varies widely among demographic subgroups. The factors associated with high risk are relatively young age (18-24), being separated or divorced, cohabiting while unmarried, being Hispanic or of a minority race, having a low income, being covered by Medicaid and having had four or more births. Factors that are associated with low abortion rates include being a born-again or Evangelical Christian, being aged 35 or older, having high income, living in a nonmetropolitan county, being married and identifying with a religion other than Catholicism.

With the exception of cohabiting, the characteristics associated with high abortion rates suggest a lack of financial and social resources and, perhaps, a lack of control over one's life. Cohabiting women have sexual intercourse more frequently than do married women,¹⁶ and they may be ambivalent about having children.

Identifying with a religion, on the other hand, suggests integration into a community that provides support and limits on behavior, as well as belief in a doctrine that probably

discourages abortion and sexual activity outside marriage. Being a born-again or Evangelical Christian is associated with a relatively low probability of having an abortion, but even so, 18% of abortion patients are born-again or Evangelical Christians. The causal relationship is not clear, however, since the characteristics that predispose a woman against sexual risk-taking may also predispose her to be born-again or to be attracted to Evangelical religious groups. The surprise, since Catholic dogma is more visibly opposed to abortion than is that of most other religions, is that identification as a Catholic does not result in a low relative abortion rate. One can speculate that the reason might be that Catholics use less effective methods of contraception, are more opposed to childbearing outside marriage or are concentrated in cities and geographic areas with high abortion rates.

Women in nonmetropolitan counties often live in small communities with more effective norms against sexual risk-taking and abortion. This and the relative inaccessibility of abortion services outside metropolitan areas may account for their low abortion rate.

The abortion indices for a number of subgroups have changed since 1987. As noted earlier, some of the difference could be associated with shifts in contraceptive behavior. Another factor may be increased acceptance of childbearing outside marriage. Among teenagers, for example, the decline in abortions was accompanied until 1991 by an increase in nonmarital childbearing. Similarly, the number of abortions obtained by women with no children has decreased, while the relative number among women with two children has gone up. These changes are consistent with the hypothesis that unmarried women are increasingly willing to carry pregnancies to term unless they already have one or two children.

Hispanic women's rising relative abortion rate suggests a need for further research to both confirm the finding and explore the reasons. One can hypothesize that as young Hispanic women become acculturated, they initiate sexual activity at an earlier age and experience more unintended pregnancies. Also, new immigrants may include women with children who wish to terminate childbearing or space their births and turn to abortion because they are unaccustomed to using modern contraceptive methods or have limited access to family planning services.

The observed increase in the proportion of abortion patients who were using a contraceptive method during the month they became pregnant and the shift in methods used could have been affected by changes in the relative effectiveness with which the various methods are used or in the proportions of unintended pregnancies terminated by abortion; however, shifts of this magnitude probably reflect changes in contraceptive use patterns in the population. Data from the 1990 NSFG telephone reinterview survey showed similar patterns of increased condom use among 15-19-year-old, black, never-married, less-educated and low-income women, and decreased pill use among 15-17-year-old, black, never-married and low-income women.¹⁷

Thus, couples appear to have heard the message that they should use condoms to prevent infection with the human immunodeficiency virus and other sexually transmitted diseases. Such a change could increase the unintended pregnancy rate if women switch from the pill or other effective methods, but judging from women having abortions, this has not happened. Among abortion patients, most of the additional condom users replaced women using other barrier methods or no method at all, while the drop in pill users was small.

These findings could indicate that the decrease in the national abortion rate evident in 1992

may have resulted, at least in part, from fewer unintended pregnancies due to greater contraceptive use and net use of more effective methods.¹⁸ In particular, the reduced proportion of nonusers and withdrawal users among teenagers could account for some of the fall in the abortion rate among this age-group if the experience of abortion patients reflects that of the population generally. Similarly, the shift from pill to condom use among black women could help account for the relative increase in the abortion rate of this group.

To further lower the abortion rate, the focus should continue to be on reducing the number of couples who use no contraceptive method at all. Most of those who were not using a method had used one in the past and conceived within a very short period after discontinuing use. Thus, it is very important for couples to avoid lapses in method use and to immediately adopt another method when they discontinue one.

Next in importance would be to improve the effectiveness with which condoms are used, since one-third of abortion patients experienced the failure of this method. Because most of these failures probably resulted from inconsistent use, the need for protection at every act of intercourse should be stressed.

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*For each item requiring imputation, correlations and cross-tabulations were used to identify the variables most strongly associated with it. Respondents were sorted according to these variables in the order of the strength of the item's association with the variable to be imputed, so that similar cases were adjacent to one another in the file. A missing value was then replaced by the value of the preceding case in the file.

**Unpublished tables showing adjusted characteristics of abortion patients for 1989-1991 are available from the authors. For a description of the adjustments made to CDC data, see reference 1.

***For a mathematical proof that the ratio of these proportions is the same as the ratio of the subgroup's abortion rate to the overall abortion rate, see reference 2, p. 162.

****The Gallup interview asks, "What is your religious preference--Protestant, Roman Catholic, Jewish or an Orthodox religion such as the Greek or Russian Orthodox Church?" Our questionnaire asked, "Are you Protestant, Roman Catholic, Jewish or something else?" Answer categories included "Other (specify)" and "None." Some Gallup poll respondents may give the religion in which they were raised even if they are no longer affiliated, while women in an abortion facility may be more likely to say they have no religion. In either case, the abortion index for women with no affiliation would be overestimated, while the indices for those identified with a religion would be underestimated.

‡The Gallup question combines "born-again" with "Evangelical," a term used by some mainstream Protestant denominations. In a 1993 experiment, Gallup found that the number of positive responses was reduced by 34% when "Evangelical" was omitted from the question. Thus, about 30% of women 18-44 consider themselves born-again Christians. (See: L. McAneny and L. Saad, "Strong Ties Between Religious Commitment and Abortion Views," *Gallup Poll Monthly*, Apr. 1993, pp. 35-43.)

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Unintended Pregnancy in the United States

By Stanley K. Henshaw

Context: Current debates on how to reduce the high U.S. abortion rate often fail to take into account the role of unintended pregnancy, an important determinant of abortion.

Methods: Data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, are used to estimate 1994 rates and percentages of unintended birth and pregnancy and the proportion of women who have experienced an unintended birth, an abortion or both. In addition, estimates are made of the proportion of women who will have had an abortion by age 45.

Results: Excluding miscarriages, 49% of the pregnancies concluding in 1994 were unintended; 54% of these ended in abortion. Forty-eight percent of women aged 15-44 in 1994 had had at least one unplanned pregnancy sometime in their lives; 28% had had one or more unplanned births, 30% had had one or more abortions and 11% had had both. At 1994 rates, women can expect to have 1.42 unintended pregnancies by the time they are 45, and at 1992 rates, 43% of women will have had an abortion. Between 1987 and 1994, the unintended pregnancy rate declined by 16%, from 54 to 45 per 1,000 women of reproductive age. The proportion of unplanned pregnancies that ended in abortion increased among women aged 20 and older, but decreased among teenagers, who are now more likely than older women to continue their unplanned pregnancies. The unintended pregnancy rate was highest among women who were aged 18-24, unmarried, low-income, black or Hispanic.

Conclusion: Rates of unintended pregnancy have declined, probably as a result of higher contraceptive prevalence and use of more effective methods. Efforts to achieve further decreases should focus on reducing risky behavior, promoting the use of effective contraceptive methods and improving the effectiveness with which all methods are used.

Family Planning Perspectives, 1998, 30(1):24-29 & 46

The relatively high rate of unintended pregnancy in the United States¹ has received increasing attention as the immediate cause of both abortion and unplanned birth. For example, the Institute of Medicine recently published a report that summarized the consequences of unintended pregnancies that are carried to term and urged the adoption of a new national goal that all pregnancies be planned.² Improved fertility control would allow women and couples to have children when they feel best prepared socially and financially to assume the responsibilities of parenting.

The most accurate national estimates of unplanned birth have been based on the National Surveys of Family Growth (NSFG), a series of nationally representative surveys that collect detailed reproductive and contraceptive histories and related information from women of reproductive age. A study based on the 1988 NSFG estimated that 57% of pregnancies in 1987 (excluding miscarriages) were unintended; that is, they ended in induced abortion, the woman had wanted no children at that time or she had wanted no more children ever.³ A study of births to ever-married women found that the proportion of births that were unplanned decreased from 38% in 1969-1973 to 32% in 1978-1982, then increased again to 35% in 1984-1988.⁴ Another study comparing the 1982 and 1988 NSFG survey results found that there had been no change in the unintended pregnancy rate between 1982 and 1987, but that the unintended birth rate had increased from 25 per 1,000 women aged 15-44 to 27 per 1,000, while the abortion rate fell by a similar amount.⁵ An earlier study based on the 1982 NSFG concluded that 46% of women aged 15-44 at the time of the survey had experienced one or more unintended pregnancies and that at 1982 rates, 46% would have at least one abortion by age 45.⁶

The publication of data from the 1995 NSFG⁷ provides information on the intendedness of births during the five years preceding the 1995 survey interviews, and can be used as the basis of an updated report on unintended pregnancy. In this article, we assess the prevalence of unintended pregnancy during this period, the changes from 1987 to 1994 and the effect of changes in unintended pregnancy rates on rates of abortion and unplanned birth.

Data and Methodology

Data from the 1995 NSFG and from other sources are used to present estimates, for 1994, of the percentage of births and pregnancies that were unintended, the intended and unintended pregnancy rates, and the proportion of women who have ever had an unintended birth, an abortion or both. In addition, we have calculated the proportion of women who, at 1992 rates, will have had an abortion by age 45. For this analysis, unintended pregnancies were estimated as the sum of abortions and of births resulting from pregnancies reported as having been unintended.

Births

The most recent national data on the planning status of births come from the NSFG, a periodic fertility survey. In addition to the 1995 survey, we also use data from NSFGs conducted in 1982 and 1988.

The 1995 NSFG interviewed a nationally representative probability sample of 10,847 civilian women aged 15-44.⁸ Interviews were conducted between January and October 1995 and included questions on the planning status of each pregnancy experienced by a respondent. Following the NSFG definition, births were categorized as unplanned if the woman had been practicing contraception when she became pregnant, if she had not wanted to become pregnant until a later time or if she had wanted no more children ever. The pregnancy was considered intended if the woman had not been practicing contraception and reported that she had not cared whether she became pregnant. The small number of births for which intention status was undetermined (0.3%) were distributed proportionally.

This information was used to determine the proportion of unplanned births among NSFG respondents in the five years preceding the interview. We chose the five-year period to ensure that the sample size would be large enough to yield a stable proportion. We estimated

the number of unplanned births in the United States by multiplying the resulting proportion with the number of births reported in 1994 by the National Center for Health Statistics (NCHS).⁹

We also estimated unplanned births for 1994 according to the mothers' age, marital status, poverty status, race, ethnicity and contraceptive use during the month of conception. Since the number of births by poverty status is not published by the NCHS, we used the poverty distribution of births, as tabulated from the NSFG. Births to unmarried women are reported by the NCHS, but we used NSFG tabulations to further categorize these women as formerly married or never-married.

For 1981 and 1987, the proportions of unplanned births were taken from published 1982 and 1988 NSFG results¹⁰ and applied to the numbers of births in 1981 and 1987.¹¹ While the NSFG coded the woman as married or unmarried for each birth, it did not include a category for formerly married women. For this reason, we were unable to calculate marital status for 1981.

Finally, using the 1995 NSFG data, we estimated the proportion of U.S. women in 1994 who had ever had an unplanned birth. In the interests of simplicity and comparability with other published data, the results for all analyses are presented according to the age and marital status of the woman at the time of the birth or abortion, rather than her age and marital status at the time of conception. Similarly, the year shown is the year of pregnancy outcome, not the year of conception.

Abortions

In calculating the number of unintended* pregnancies, it was assumed that all pregnancies ending in abortion were unwanted, although a small proportion of abortions may have occurred among initially wanted pregnancies. This may have happened for any number of reasons, including health problems experienced by the woman or the fetus or changes in the woman's circumstances, sometimes resulting from the loss of her partner or lack of support.¹²

To calculate the number of unintended pregnancies in 1994, we needed an estimate of the total number of abortions that occurred during the year and data on the characteristics of women who had abortions. The total number of abortions performed nationally is compiled through periodic surveys of abortion providers conducted by The Alan Guttmacher Institute.¹³ However, this provided abortion estimates only through 1992, the most recent year covered by the surveys. For 1993 and 1994, we projected totals from trends in the number of abortions in published and unpublished reports from state health statistics agencies. We used information only from states with consistent data collection procedures in the two adjacent years (42 states and the District of Columbia to project 1993 totals from the 1992 data, and 43 states and the District of Columbia to project 1994 totals from the 1993 data).

The age, marital status, race and ethnicity of women who had had abortions were based on percentage distributions compiled from state health department reports by the Centers for Disease Control and Prevention (CDC),¹⁴ with adjustments for year-to-year changes in the reporting states.¹⁵ For 1994, we separated unmarried women who had had abortions into subcategories of never-married and formerly married women and derived the distribution of

abortions by women's poverty status according to data from a 1994-1995 national survey of 9,985 abortion patients.¹⁵ For 1987, we took the distribution of abortions by marital status from a similar survey of 9,480 abortion patients in that year.¹⁶

Because abortions are underreported in population surveys,¹⁷ we decided not to use NFSG data on the number of women in each age-group who had ever had an abortion, a procedure that would have resulted in a serious underestimate. Instead, we made estimates from national abortion statistics, a complicated task since a woman aged 35 in 1994 could have had an abortion in any year since 1973, placing her in a number of possible age-groups. In addition, we wished to avoid counting more than once the many women who have had more than one abortion.

The first step in estimating the number of women in each age-group who have had an abortion was to estimate the number of abortions that occurred in each year according to single year of age. We started with the number of abortions by five-year age-groups (with single-year groupings for teenagers) for each year during 1973-1994, derived from CDC reports with adjustments as described above. To distribute the five-year groups to single years of age, we used microdata tapes compiled by the NCHS for 1980, 1983, 1985, 1986 and 1988-1992.¹⁸ Each tape contains data on more than 280,000 abortions in 12 or more states. We used tabulations of these abortions by single year of age to break down national five-year age-groups into single-year categories. For years lacking an NCHS tape, we interpolated or projected figures.

We also used the tape tabulations to calculate for each year during 1973-1994 the proportion of first-time abortions within each single-year age-group. First, we multiplied the number of abortions by the proportions we had derived from the tapes in order to arrive at an initial estimate for each year of first abortions for each single year of age. We then adjusted the numbers of first abortions in each single-year age category so that the sum for each year was equal to the total number of first abortions previously estimated for that year from CDC data. To estimate the cumulative number of first abortions that took place during 1973-1994 for each age cohort, we added together the number of first abortions that each age-group would have experienced for each year during this period. We then divided this total by the number of women in that age-group in the population in 1994 to arrive at the proportion of U.S. women in each age-group who had ever had an abortion.

Our estimates of the number of first abortions are subject to several possible sources of error: The states included in the NCHS tapes may not have been completely representative of all women having abortions; some women may not have reported their prior abortions to the abortion provider; some of the women who had first abortions died before 1994 and should not have been counted; and some immigrants may have had abortions before coming to the United States.¹⁹ Nevertheless, the results provide an approximate picture of the past abortion experience of U.S. women since the 1973 *Roe v. Wade* decision.

Unintended Pregnancy

We estimated the proportion of women who have ever had an unintended pregnancy by first adding the number of women who had had an unplanned birth to the number who had had an abortion, and then subtracting those who were counted twice because they had had both an unplanned birth and an abortion. Tabulations of the NFSG indicate that the proportion of women who have had an unintended birth and also reported having had an abortion ranged from 9% among women aged 15-19 to 28% among women aged 30-34. Since comparisons

with national data indicate that the actual number of abortions experienced is about 56% higher than the number reported in the NSFG for the period 1976-1994,¹⁸ we used this figure as a correction factor and adjusted the proportion experiencing both unintended birth and abortion upward for each age-group. Since the rate of abortion underreporting was the same for women younger than 35 and those aged 35-44, we used the same correction factor in all age-groups.¹⁹

Miscarriages

Except where otherwise specified, we excluded miscarriages from all calculations of the number of pregnancies and of pregnancy rates. With miscarriages omitted, the proportion of unintended pregnancies that ended in abortion reflects actual decisions to terminate or continue pregnancies. In addition, it assures that all tables in this article are consistent, since it would be difficult to calculate the proportion of women who have ever had an unintended pregnancy while at the same time taking into account the overlap between women who have had unintended pregnancies that ended in miscarriage, birth and abortion. (However, the number of miscarriages after 6-7 weeks of pregnancy--the point at which miscarriages are likely to be noted by the woman--can be estimated by adding 20% of births to 10% of abortions.²⁰ Miscarriages may also be estimated using NSFG data.²¹)

Results

Rates and Outcomes

Approximately 3.95 million births and 1.43 million abortions occurred in 1994, for a total of 5.38 million pregnancies, not including miscarriages. (Use of the estimation procedure mentioned above produces an estimated 930,000 miscarriages during the year as well.) The largest number of pregnancies occurred among women aged 20-29, among currently married women, among those with an income 200% or more of the federal poverty level, and among white and non-Hispanic women (Table 1).

Table 1. Estimated number of pregnancies (excluding miscarriages), percentage distribution by intention, and selected measures of unintended pregnancy, all by characteristic, 1994

Characteristic	No. of pregnancies	% distribution of pregnancies				% of births that were unintended	% of pregnancies that were unintended
		Intended births	Unintended births	Abortions	Total		
Total	5,383,800	50.8	23.0	26.6	100.0	30.8	49.2
Age at outcome							
<15	25,100	18.3	33.2	48.5	100.0	64.5	81.7
15-19	781,900	22.0	42.7	35.3	100.0	66.0	78.0
15-17	306,100	17.3	46.5	36.2	100.0	72.9	82.7
18-19	475,800	25.0	40.2	34.8	100.0	61.7	75.0
20-24	1,479,500	41.5	26.2	32.3	100.0	38.7	58.5
25-29	1,405,200	60.3	17.2	22.5	100.0	22.2	39.7
30-34	1,111,400	66.9	14.6	18.4	100.0	18.0	33.1
35-39	482,400	59.2	17.9	23.0	100.0	23.2	40.8

>=40y	98,300	49.3	17.9	32.8	100.0	26.7	50.7
Marital status at outcome							
Currently married§	3,003,900	69.3	19.3	11.3	100.0	21.8	30.7
Formerly married	356,700	37.5	21.8	40.7	100.0	36.8	62.5
Never-married	2,023,100	22.3	31.0	46.7	100.0	58.2	77.7
Poverty status**							
<100%	1,358,000	38.6	31.3	30.1	100.0	44.8	61.4
100-199%	1,292,500	46.8	27.7	25.4	100.0	37.2	53.2
>=200%	2,733,200	58.8	15.9	25.4	100.0	21.3	41.2
Race							
White	3,981,700	57.1	21.2	21.6	100.0	27.1	42.9
Black	1,130,700	27.7	28.6	43.7	100.0	50.8	72.3
Other	271,400	50.0	22.0	28.0	100.0	30.5	50.0
Ethnicity							
Hispanic	900,200	51.4	22.4	26.1	100.0	30.4	48.6
Non-Hispanic	4,483,600	50.7	22.6	26.7	100.0	30.9	49.3
*Pregnancy rates for this category are expressed as per 1,000 women aged 15-44, except for rates for women aged 14. †Numerator for rates is women aged 40 and older; denominator is all women. **Percentage of federal poverty level at time of interview. In 1994, the federal poverty level was 14,829. ‡Note: Intention status of births is based on births in the five years before the 1995 interview.							

During the five years preceding the 1995 NSFG interview, 31% of births were reported as unintended--that is, the woman did not want to have children when she did (21%) or wanted no more births ever (10%). Applying the same proportions to 1994 births, we estimated that 1.22 million births resulted from unintended pregnancies. Adding abortions, there were 2.65 million unintended pregnancies, or 49% of all pregnancies for that year. (If we include an estimated 390,000 miscarriages that would have otherwise ended in abortion or unintended birth, we find that a total of 3.04 million unintended pregnancies occurred during 1994.) Of all pregnancies in 1994 (excluding miscarriages), 23% ended in unintended births and 27% in abortions. Thus, among women who experienced an unintended pregnancy in 1994 (excluding miscarriages), 54% had an abortion and 46% carried the pregnancy to term.

Forty-eight percent of the women who had an unplanned birth had been using a contraceptive method during the month they became pregnant,** as had 58% of those who had abortions (not shown). For all unintended pregnancies combined, slightly more than half (53%) of the women had been using a method. Of the contraceptive users, 58% ended their pregnancies by abortion, compared with 49% of nonusers who had accidental pregnancies. (When the estimated number of unintended pregnancies that ended in miscarriage is included, the percentage of women who were using a method remains at 53%, but among contraceptive users, we estimate that 51% had abortions, 37% had births and 12% had miscarriages; among nonusers, we estimate that 43% had abortions, 44% had births and 13% had miscarriages.)

Thus, contraceptive users appear to have been more motivated to prevent births than were nonusers, although many nonusers did have abortions.

The proportion of all pregnancies that were unintended varied sharply by age, with teenagers younger than 18 having the highest percentage (82-83%). The proportion decreased with rising age, dropping to 33% among women aged 30-34, and then increased again, reaching 51% among women aged 40 and older. Some 44% of teenagers aged 15-17 ended their unintended pregnancies by abortion, the lowest proportion in any age-group. (The relatively high proportion among women younger than 15 is misleading because it excludes the pregnancies of 14-year-olds that ended in births at age 15. It also excludes pregnancies to 14-year-olds that ended in abortion at age 15, but there are relatively few of these.) The proportion was also relatively low for women aged 18-19 (46%), and was highest among women older than 40 (65%).^{*Y}

The unintended pregnancy rate shows that for every 1,000 women aged 15-44, about 45 had an accidental pregnancy during 1994 (or nearly 5%). Among women aged 15-17, the rate was similar to that for all women. It peaked at 105 per 1,000 among women aged 18-19, then dropped sharply with age. At these rates, a cohort of 100 women will have experienced 142 unintended pregnancies, or about 1.42 per woman, by the time they are 45 (not shown).

The intended pregnancy rate was about the same as the unintended rate (46 per 1,000), having increased from 40 per 1,000 in 1987 and 43 per 1,000 in 1981 (not shown). The age pattern of intended pregnancy, however, was very different from that of unintended pregnancy: Intended pregnancy was much higher than unintended pregnancy among women aged 25-39 and much lower than unintended pregnancy among teenagers. Each year, 1% of all women aged 15-17 had an intended pregnancy.

Among married women, 31% of pregnancies were unintended, compared with 63% among formerly married women and 78% among never-married women. Only 37% of married women who had unintended pregnancies ended them by abortion, compared with 60-65% of unmarried women. The pregnancy rate among never-married women (91 per 1,000) was about the same as that of married women (95 per 1,000). The outcomes of these pregnancies reflect differences in intention status for these groups, however: Almost half of pregnancies among formerly and never-married women ended in abortion (47% and 41%, respectively), compared with only 11% of those among married women.

Women's poverty status (defined as the ratio of family income to the federal definition of poverty)^{*Y} was strongly associated with the unintended pregnancy rate but only weakly associated with the rate of intended pregnancy. Among women in poverty, pregnancies were more likely than among higher income women to be unintended and to end in unplanned births, and were slightly more likely to end in abortions. The overall pregnancy rate declined with increasing income, and this trend resulted mainly from the higher rate of unintended pregnancy among poor women. The proportion of poor women's unintended pregnancies that ended in abortion was similar to the proportion among women living at 100-199% of the poverty level, and was less than that among women whose income was 200% or more of the poverty level.

The differences between white and black women generally paralleled those between high- and low-income women: Compared with white women, black women had a higher pregnancy rate. The higher pregnancy rate for black women resulted from an unintended

pregnancy rate that was almost three times that of white women. Because black women's unintended pregnancy rate was so high, the proportion of these women's pregnancies that ended in abortion (44%) was much higher than that of white women (22%).

On all measures, women of other races fell between white and black women, usually closer to white women. Hispanic women had a much higher rate of both intended and unintended pregnancy than did non-Hispanic women, but the percentage of unintended pregnancies and births and the distribution of outcomes were almost identical for Hispanic and non-Hispanic women.

Trends

There have been significant changes over time in the frequency of unintended pregnancy and in the resolution of such pregnancies, especially since 1987. Between 1981 and 1987, the unintended pregnancy rate changed little, but from 1987 to 1994, the rate dropped 16%, from 54 per 1,000 to 45 per 1,000 (Table 2). As a result, the rates of both unintended births and abortions fell between 1987 and 1994, but the drop was greater for unintended births (6 per 1,000) than for abortions (3 per 1,000). Consequently, the proportion of unintended pregnancies ended by abortion increased from 50% to 54%.

Table 2. Estimated rates of unintended pregnancies, unintended births and abortions per 1,000 women, age and marital status, and percentage of unintended pregnancies ended by abortion, by characteristic, 1981, 1987 and 1994												
Characteristic	Unintended pregnancy			Unintended birth			Abortion			% ended by abortion		
	1981	1987	1994	1981	1987	1994	1981	1987	1994	1981	1987	1994
Total	54.2	53.5	44.7	25.0	26.6	20.9	29.2	26.9	24.1	53.9	50.3	54.0
Age at outcome												
15-19	78.1	79.3	71.1	35.2	37.1	38.9	42.9	42.2	32.2	54.9	53.2	45.3
20-24	93.6	102.7	96.0	42.3	50.2	43.0	51.4	52.5	53.0	54.8	51.1	55.2
25-29	60.6	66.1	58.4	29.3	35.4	25.3	31.3	30.8	33.1	51.6	46.5	56.7
30-34	37.0	37.3	33.1	19.3	19.3	14.6	17.7	17.9	18.4	47.8	48.2	55.7
35-39	15.0	18.8	17.8	5.5	9.0	7.8	9.5	9.8	10.0	63.5	52.2	56.3
>=40*	4.3	5.3	5.0	0.9	2.4	1.8	3.4	2.9	3.2	78.2	54.3	64.7
Marital status at outcome												
Currently married [†]	u	41.5	29.2	u	29.8	18.4	u	11.7	10.8	u	28.2	37.0
Formerly married	u	54.6	40.4	u	19.0	14.1	u	35.7	26.3	u	65.3	65.1
Never married	u	71.5	70.8	u	23.2	28.2	u	48.2	42.5	u	67.5	60.1
*Numerator for rates is women aged 40 and older; denominator is women aged 40-44. [†] Includes separated women. Notes: All measures exclude miscarriages. The intention status of births is based on births in the five years before the interviews in 1988 and 1995 and in the four years before the 1982 interview. u=unavailable.												

The changes differed markedly by age-group, especially when teenagers were compared with women aged 20 and older. Between 1981 and 1987, the unintended pregnancy rate and birthrate changed little among teenagers but increased among all women aged 20 and older, except among women aged 30-34. Changes in abortion rates were very small during this period. From 1987 to 1994, the rate of unintended pregnancy fell among all age-groups, although the change was small among women aged 35 and older. Among teenagers, the drop in unintended pregnancy affected only the abortion rate, which fell by 24% (from 42 per 1,000 to 32 per 1,000), while the rate of unintended births actually increased slightly (from 37 per 1,000 to 39 per 1,000). Among all other age-groups, the abortion rate increased slightly or stayed the same, while the rate of unintended births fell significantly as a consequence of the reduced rate of unintended pregnancy. In 1994, teenage women were less likely than women in any other age-group to end an unintended pregnancy by abortion, whereas in earlier periods teenagers have been similar to other women in this respect.

Between 1987 and 1994, currently and formerly married women experienced reductions in unintended pregnancy that were reflected in decreases both in the rate of unintended birth and in that of abortion. Among married women, the proportion of unintended pregnancies that ended in abortion increased from 28% to 37%. Never-married women, on the other hand, reported an increase in unintended births that was approximately equal to the decrease in abortions in this group, and the proportion of unintended pregnancies that ended in abortion declined.

All three income groups experienced a decrease in the proportion of pregnancies that were unintended (not shown).²² The proportion of unintended pregnancies that ended in abortion remained about the same among women in the lowest income group, decreased among those in the middle income group and increased sharply among women in the highest income category.

Lifetime Experiences

Over their lifetime, the proportion of women experiencing an unintended pregnancy is substantial, even when the proportion in any one year is small. Of the women aged 15-44 who were surveyed in the 1995 NFSG, 28% indicated that they had had one or more unplanned births, and based on national abortion statistics, 30% of women had had one or more abortions (Table 3). The probability of having experienced an unplanned birth increased with age, largely because of the increased years of exposure to pregnancy risk. By the time they were 40-44, 38% of the women surveyed had had this experience.

Table 3. Percentage of women who have ever had at least one unplanned birth, abortion or unintended pregnancy, by age-group, 1994				
Age	>=1 unplanned births	>=1 abortions*	Both birth and abortion	>=1 unintended pregnancies ^Y
Total	28.4	29.9	10.6	47.7
15-19	6.1	7.0	0.9	12.2
20-24	22.5	26.3	7.4	41.4

30-34	33.7	40.2	14.8	59.2
35-39	36.6	38.3	14.9	60.0
40-44	38.1	25.0	12.7	50.4
*Since 1973. †Excludes miscarriages.				

Similarly, the probability of having had an abortion also increased with age, rising from 7% among women aged 15-19 to 40% among women aged 30-34. The proportion was lower among women older than 34 because this research did not attempt to include abortions before 1973, when these women experienced their highest-risk years (ages 15-24). Overall, 11% of all women had had both at least one unplanned birth and at least one abortion. Among women in their 30s, this proportion was 15%.

About 48% of all women aged 15-44 had ever had an unintended pregnancy (either an unplanned birth or an abortion, or both). The percentage increased with age, to a high of 60% among women 35-39. Although the percentage was lower among women aged 40-44, this figure may be understated, again because neither legal nor illegal abortions that occurred before 1973 were counted in this estimate.

Although we know how many women in each age-group had already had an unintended pregnancy, we cannot say exactly how many will have one by age 45, because of the difficulties of estimating the proportion of women having a first abortion who have previously had an unplanned birth and, of those having an unplanned birth, the proportion who have had an abortion. However, we were able to make lifetime abortion estimates at 1992 rates, the most recent year for which data were available (Table 4).*§;

Table 4. Abortion rate per 1,000 women and percentage of abortions that were first abortions, and first-abortion and cumulative first-abortion rates, by year, all according to age-group

Age	Abortion rate in 1992	% that were first abortions in 1992	First-abortion rate		Cumulative first-abortion rate*	
			1982	1992	1982	1992
Total	25.9	.530	17.8	13.7	na	na
<15†	7.6	.942	7.8	7.2	7.8	7.2
15-17	23.1	.855	26.0	19.7	85.8	66.4
18-19	53.8	.722	45.4	38.9	176.6	144.1
15-19	35.5	.760	34.1	27.0	176.6	144.1
20-24	56.3	.541	30.3	30.5	328.1	296.5
25-29	33.9	.419	15.7	14.2	406.6	367.5
30-34	19.0	.393	7.1	7.5	442.1	404.8

35-39	10.4	.405	2.8	4.2	456.1	425.9
40-44 ^y	3.2	.453	0.7	1.4	459.6	433.1
<p>*Number having an abortion by end of specific age-period, per 1,000 women, at current rates. ^yDenominator for rates is women aged 14. ^yNumerator for rates is women aged 40 and older; denominator is women aged 40-44. <i>Note:</i> na=not applicable. <i>Sources:</i> 1982 DATA--See reference 6.</p>						

We estimated the first-abortion rate by applying the 1992 proportion of first abortions for each age-group to the abortion rate for that age-group. The cumulative first-abortion rate indicates the number of women per 1,000, at 1992 rates, who will have had a first abortion by the time they reach the end of the age range. At these rates, 14% of women can expect to have had an abortion before age 20, 37% by age 30 and 43% by age 45.^{Y*}

The 1992 cumulative lifetime first-abortion rate was slightly lower than the 1982 cumulative rate (46%),²³ and the rate may be still lower today, since abortion rates fell somewhat between 1992 and 1994. The drop between 1982 and 1992 was almost entirely the result of the lower first-abortion rate among teenagers, which fell by seven percentage points; the first-abortion rate among other age-groups changed by no more than two percentage points.

Discussion

Although it is well known that unintended pregnancy is common in the United States, the statistics presented in this article show just how widespread the experience is: Half of all pregnancies are unintended; 28% of women aged 15-44 have had an unplanned birth and 30% have had an abortion; 60% of women in their 30s have had an unplanned birth or an abortion; and, at 1992 rates, 43% of women will have had an abortion by age 45. Some of the women who are most prone to unintended pregnancy, especially unmarried and low-income women, are those who may have the greatest difficulty caring for an unanticipated child.

In spite of the disruption that can be caused by an unplanned birth, only about half of unintended pregnancies are terminated by abortion. A majority of married women (63%) continue their unintended pregnancies, possibly because they find it easier to accommodate an additional child than do unmarried women. However, 35% of formerly married women and 40% of never-married women also continue their unplanned pregnancies.

Between 1987 and 1994, the rate of unintended pregnancy fell from 54 pregnancies per 1,000 women of reproductive age to 45 per 1,000, a decrease of 16%. A likely explanation for the decline in unintended pregnancy is an increase in widespread and effective contraceptive use. The 1995 NSFG data show that condom use has increased significantly, and that the proportion of contraceptive nonusers among women at risk of unintended pregnancy has gone down.²⁴ Another possible factor is the availability of two new highly effective contraceptives, the implant and the injectable. In part because Medicaid pays for these methods, many of the women who adopted them were at especially high risk of unintended pregnancy--even when they were using other reversible methods. Therefore, use of the new methods may have prevented a disproportionate number of pregnancies.

Overall, the drop in unintended pregnancy between 1987 and 1994 is reflected in decreases

in the rates of both unplanned birth and abortion. Further progress is needed, however. In view of the lower rates of unintended pregnancy in other developed countries,²⁵ such progress should be possible.

Among women aged 20 and older, the reduction in unintended pregnancy resulted in lower rates of unplanned birth. Abortion rates in this group changed little or increased slightly. Thus, the percentage of unintended pregnancies ended by abortion increased, indicating that women and couples had become less willing to accept unplanned births. One reason for the change is that a higher proportion of women in each age-group were not currently married. Among unmarried women, 60-65% resolved unintended pregnancies by abortion, compared with 37% among married women. Of women aged 25-29, the proportion who were currently married and living with their husband fell from 59% in 1987 to 53% in 1994.²⁶ Even within the married group, however, more women ended their unintended pregnancies by abortion in 1994 than did so in 1987. One possible reason may be married couples' increased reliance on the woman's earnings.

The pattern among teenagers is remarkably different. Among women aged 15-19 who had an unwanted pregnancy, the proportion who ended these pregnancies by abortion fell from 53% to 45%. The abortion rate declined 24%, while the rate of unplanned birth did not decline at all--and may have increased slightly. In the absence of data, any explanation of the differences between teenagers and other age-groups is speculative. One hypothesis is that teenagers may have been influenced by antiabortion messages. Other possible reasons are decreased access to abortion services, barriers posed by parental involvement statutes, and use of better contraceptive methods (such as the injectable and implant) by those teenagers who are strongly motivated to avoid childbearing, leaving unplanned pregnancies more concentrated among those less motivated to avoid childbearing.

Whether they end in abortion or unplanned birth, unintended pregnancies come at a cost both to the individuals involved and to the larger society. Reduction of unplanned pregnancy can only be achieved by decreasing risky behavior, promoting the use of effective contraceptive methods and improving the effectiveness with which all methods are used. More research is needed on the best ways to accomplish these goals, but we know that sensible strategies are to improve the accessibility of contraceptive services, to dispel misconceptions about the health risks of contraception and to make emergency contraception easily available and widely known.

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§The number of immigrants exceeded the number of deaths, resulting in an increase by 3-4% of the number of women in each age cohort between 1980 and 1990.

**Based on NFSG tabulations of births that were conceived after January 1, 1991, and that took place before the interview. For abortion data, see reference 15.

*YThese figures are based on the age of the woman when the pregnancy ended, not her age at conception. Adjustment to age at conception would lower the proportions for women younger than 20 and raise them for women older than 30.

*yIn 1994, the federal poverty level was \$17,020 for a family of four.

*§Information on the proportion of first abortions by age is unavailable for years since 1992. For calculating the lifetime experience of abortion for Table 3, we assumed that the 1993 and 1994 proportions of first abortion were similar to those for 1992, since small errors would have little effect on the results. The cumulative first abortion rate, however, depends entirely on these proportions, which are only accurate for 1992.

Y*In the future, one can expect that for women having abortions at age 35 or older, a lower proportion will be having a first abortion, since a greater proportion of their reproductive lives will have occurred while legal abortion has been available. If we assume that the proportion of first abortions was .35 for women aged 35-39 and .30 for women aged 40-44, the cumulative abortion rate for women aged 45 will be 428 per 1,000, similar to the rate of 433 per 1,000, shown in Table 4.

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Complications of Interval Laparoscopic Tubal Sterilization: Findings From the United States Collaborative Review of Sterilization

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Objective: To estimate the risk of intraoperative or postoperative complications for interval laparoscopic tubal sterilizations.

Methods: We used a prospective, multicenter cohort study of 9475 women who had interval laparoscopic tubal sterilization to calculate the rates of intraoperative or postoperative complications. The relative safety of various methods was assessed by calculating overall complication rates for each major method of tubal occlusion. Method-related complication rates also were calculated and included only complications attributable to a method of occlusion. We used logistic regression to identify independent predictors of one or more complications.

Results: When we used a more restrictive definition of unintended major surgery, the overall rate of complications

went from 1.6 to 0.9 per 100 procedures. There was one life-threatening event and there were no deaths. Complication rates for each of the four major methods of tubal occlusion ranged from 1.17 to 1.95, with no significant differences between them. When complication rates were calculated, the spring clip method had the lowest method-related complication rate (0.47 per 100 procedures), although it was not significantly different from the others. In adjusted analysis, diabetes mellitus (adjusted odds ratio [OR] 4.5; 95% confidence interval [CI] 2.3, 8.8), general anesthesia (OR 3.2; CI 1.6, 6.6), previous abdominal or pelvic surgery (OR 2.0; CI 1.4, 2.9), and obesity (OR 1.7; CI 1.2, 2.6) were independent predictors of one or more complications.

Conclusion: Interval laparoscopic sterilization generally is a safe procedure; serious morbidity is rare. (Obstet Gynecol 2000;96:997-1002. © 2000 by The American College of Obstetricians and Gynecologists.)

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Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy

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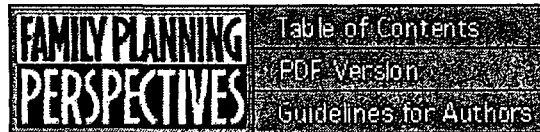
The complication rate among 282 women undergoing interval tubal sterilization by laparotomy was studied as part of the prospective multicenter Collaborative Review of Sterilization. Using a standard definition of major complications, the overall complication rate was 5.7 per 100 procedures. Women experiencing complications had a significantly lengthened postoperative recovery period before the resumption of normal activities. Important risk factors for complications included diabetes, cigarette smoking, previous abdominal or pelvic surgery, and a history of pelvic inflammatory disease. Women with an initial abdominal incision of 7 cm or longer had three times the complication rate of women with shorter incisions. These results provide objective evidence that, for tubal sterilizations, minilaparotomy (laparotomy with a small abdominal incision) is associated with lower morbidity than is conventional laparotomy. (*Obstet Gynecol* 62:180, 1983)

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Tubal Sterilization in the United States, 1994-1996

By Andrea P. MacKay, Burney A. Kieke, Jr., Lisa M. Koonin and Karen Beattie

Context: Although the number and rate of tubal sterilizations, the settings in which they are performed and the characteristics of women obtaining sterilization procedures provide important information on contraceptive practice and trends in the United States, such data have not been collected and tabulated for many years.

Methods: Information on tubal sterilizations from the National Hospital Discharge Survey and the National Survey of Ambulatory Surgery was analyzed to estimate the number and characteristics of women having a tubal sterilization procedure in the United States during the period 1994-1996 and the resulting rates of tubal sterilization. These results were compared with those of previous studies to examine trends in clinical setting, in the timing of the procedure and in patient characteristics.

Results: In 1994-1996, more than two million tubal sterilizations were performed, for an average annual rate of 11.5 per 1,000 women; half were performed postpartum and half were interval procedures (i.e., were unrelated by timing to a pregnancy). All postpartum procedures were performed during inpatient hospital stays, while 96% of interval procedures were outpatient procedures. Postpartum sterilization rates were higher than interval sterilization rates among women 20-29 years of age; interval sterilization procedures were more common than postpartum procedures at ages 35-49. Sterilization rates were highest in the South. For postpartum procedures, private insurance was the expected primary source of payment for 48% and Medicaid was expected to pay for 41%; for interval sterilization procedures, private insurance was the expected primary source of payment for 68% and Medicaid for 24%. 1989, 21(5):209-212.

Conclusions: Outpatient tubal sterilizations and procedures using laparoscopy have increased substantially since the last comprehensive analysis of tubal sterilization in 1987, an indication of the effect of technical advances on the provision of this service. Continued surveillance of both inpatient and outpatient procedures is necessary to monitor the role of tubal sterilization in contraceptive practice.

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Tubal sterilization is the most commonly used method of birth control in the United States: The 1995 National Survey of Family Growth (NSFG) reported that 28% of all women 15-44 years of age currently practicing contraception relied on tubal sterilization.¹ Tubal sterilization also is a highly effective method for women choosing to permanently terminate their reproductive ability. For example, the Collaborative Review of Sterilization (CREST) study reported a first-year probability of pregnancy of 5.5 pregnancies per 1,000 sterilization procedures and a 10-year cumulative probability of 18.5 per 1,000.²

The number and rate of tubal sterilizations performed, the settings in which they are performed and the characteristics of the women obtaining sterilization procedures provide important information on contraceptive practice and trends to public health programs such as Title X, to the Health Resources and Services Administration and state family planning agencies, and to managed care organizations, health care providers, research institutions and advocacy organizations. Information on trends in sterilization rates contributes to the general knowledge of contraceptive practice in the United States and the role of sterilization within that framework. These data can inform health care programs and providers of shifts in the need for services.

No national reporting system exists to count sterilizations performed in the United States. In the past three decades, a number of studies by the Centers for Disease Control and Prevention (CDC) and EngenderHealth (formerly AVSC International) have attempted to estimate the number of procedures performed each year, by combining data from a variety of sources, including physicians who perform sterilizations, medical facilities where sterilizations are performed and comprehensive national surveys.³

Since 1965, CDC's National Center for Health Statistics (NCHS) has relied on the National Hospital Discharge Survey (NHDS) to collect data each year on inpatient surgical and nonsurgical procedures. In response to the shift of many surgical procedures to outpatient settings, in 1994 NCHS initiated the National Survey of Ambulatory Surgery (NSAS) to augment the NHDS. These two surveys provide the most comprehensive estimates available of tubal sterilizations performed in the United States. We used data from the NHDS and NSAS to estimate the number and rate of tubal sterilizations for 1994 through 1996, as well as the clinical settings, timing of procedures and characteristics of women undergoing tubal sterilization.

Methods

The data sources for this analysis were the 1994, 1995 and 1996 NHDS⁴ and

the 1994, 1995 and 1996 NSAS.⁵ These years represent the most recently available data on all tubal sterilizations in the United States; the NSAS has not been repeated since 1996.

Clinical setting was classified as hospital inpatient (i.e., involving an overnight hospital stay), hospital ambulatory surgery centers (including procedures performed in hospitals as outpatient procedures) or freestanding surgery centers.

Hospital inpatient tubal sterilization discharges were estimated using the NHDS, an annual multistage probability sample of discharges from nonfederal, short-stay hospitals in the United States. Up to seven diagnosis codes and four procedure codes were collected for each patient. Demographic and medical information was obtained either from the face sheets of sampled records or from automated sources.

We estimated the number of outpatient visits for tubal sterilization using the NSAS, a multistage probability sample of ambulatory surgery visits in hospital-based and freestanding ambulatory surgery centers and of outpatient procedures performed in hospitals. (Procedures performed in hospital ambulatory surgery centers included those performed in hospital operating rooms on an outpatient basis.)

The sample universe included surgery centers in noninstitutional, nonfederal, short-stay hospitals and freestanding facilities listed in the 1993 SMG Freestanding Outpatient Surgery Center Database. If a freestanding facility was owned by a hospital but located some distance away, was separately listed in the 1993 SMG Freestanding Outpatient Surgery Center Database and was selected into the NSAS sample from this universe, it was considered a freestanding surgery center. Facilities specializing in abortion, family planning or delivery were excluded from the survey. A maximum of seven diagnostic codes and six procedure codes were collected for each patient.

Tubal sterilization is a permanent method of birth control in which a portion of the fallopian tube is cut and either tied, clipped, cauterized or removed. For this analysis, we defined postpartum tubal sterilizations as procedures that were completed during the same hospital stay as a delivery; interval tubal sterilizations were unrelated by timing to a pregnancy or a delivery. Our analysis is restricted to women aged 20-49.

We identified postpartum tubal sterilizations using International Classification of Disease, Clinical Modification, Ninth Revision (ICD-9-CM)⁶ codes that restricted the case selection to those that matched for a vaginal or cesarean delivery (diagnosis code V27) and tubal sterilization codes (procedure codes 66.2-66.3 or procedure codes 65.6, 66.5, 66.63 or 66.97 and diagnosis code V25.2), and excluded any procedures in which the removal of the fallopian tubes was an integral part of a hysterectomy or a procedure for reasons other

than sterilization. Inpatient interval tubal sterilizations were identified similarly, excluding any matches with delivery codes. Outpatient interval procedures were identified using ICD-9-CM codes; again, we excluded any procedures in which the removal of the fallopian tubes was an integral part of a hysterectomy or a procedure for reasons other than sterilization. Postpartum sterilizations are not routinely performed in outpatient settings, because by definition, they take place less than 48 hours after a delivery.

We categorized type of delivery (vaginal or cesarean) associated with postpartum sterilization procedures from ICD-9-CM procedure codes. We also ascertained the surgical procedure for interval sterilizations using ICD-9-CM procedure codes, and categorized these procedures as laparoscopic or not laparoscopic. Additionally, information on the type of anesthesia (local or general) used in outpatient procedures was available from NSAS.

Women 20-39 years of age were grouped in five-year age intervals, while those aged 40-49 comprised a single group. For the analysis by race, we classified women as white, black, American Indian or Alaska Native, Asian or Pacific Islander, other race or unknown race. Hispanic women were classified by their reported racial group. Due to small sample sizes and large relative standard errors, we do not discuss here any race-specific information on racial groupings other than white and black. Because of the large number of discharges (NHDS) and visits (NSAS) of unknown ("not stated") race (nearly 22% of discharges and 29% of visits), we conducted a sensitivity analysis to evaluate whether apparent differences by race remained statistically significant if all women with unknown race were classified as white (the group with lower rates).

Hospitals and ambulatory surgery centers were classified by location in one of the four geographic regions of the United States, as defined by the U.S. Bureau of the Census: Northeast, Midwest, South and West. Expected primary source of payment was categorized as private insurance (including health maintenance organizations and preferred provider organizations), Medicaid and other.* Region and expected source of payment could not be analyzed by race because of the large percentage with race not stated.

We weighted sampled discharges (NHDS) and visits (NSAS) meeting the case definition to obtain national estimates. To achieve more reliable estimates, we combined the 1994-1996 data; thus, all estimates are based on data for the three-year period. The estimated number of sterilization procedures was based on an unweighted sample of 7,838 hospital records (NHDS) and 5,629 outpatient surgical records (NSAS) for the three-year period.

Rates were calculated as the number of tubal sterilizations per 1,000 women of reproductive age (ages 20-49) in the U.S. civilian resident population. Population estimates for 1994, 1995 and 1996 were computed by the U.S. Bureau of the Census, and are included in the NHDS documentation package. When computing percentage distributions for expected primary payment

source, we excluded discharges (NHDS) and visits (NSAS) with unknown primary payment source (2% of discharges and 4% of visits) from the analysis.

We computed standard errors for estimates derived from the NHDS and NSAS using SUDAAN,⁷ a software package that accounts for complex survey designs. For rates, the denominator was treated as a known quantity (without variance). NHDS and NSAS estimates were considered statistically independent in the computation of standard errors for estimates, which combined data from the two surveys.

Results

We estimate that more than two million women aged 20-49 had a tubal sterilization procedure in the United States between 1994 and 1996. An average of almost 684,000 women underwent tubal sterilization procedures each year (Table 1). The 1994-1996 rate was 11.5 tubal sterilizations per 1,000 women, and the annual rate varied little in the three-year study period.

Approximately half of all sterilizations were performed postpartum and half were interval procedures. All postpartum procedures were performed during inpatient hospital stays, whereas only 4% of interval procedures were performed on an inpatient basis (2% of all sterilization procedures). Most interval sterilizations were performed as outpatient procedures in hospital ambulatory surgery centers or in freestanding surgery centers.

Among women aged 20-29, postpartum sterilization rates were higher than interval rates, whereas the reverse was true among women aged 35-49 (Table 2). Women choosing postpartum tubal sterilization tended to be younger than women electing to have an interval procedure.

Tubal sterilization rates varied by race. Among women whose race was known, postpartum sterilization rates for black women were twice those of white women (Table 3). (For 21% of postpartum procedures, race was not available.) Postpartum rates remained significantly higher among black women than among white women after we recoded to white all cases in which race was not stated. Inpatient and outpatient interval sterilization rates among women with stated race were also higher for black women than for white women; however, the difference was not statistically significant when cases with unknown race were recoded as white.

Sterilization rates were higher in the South than in the other three regions, which had similar rates (Table 4). Regional differences in rates varied by the timing of the sterilization procedure: Postpartum rates were higher in the South than in the other regions, while outpatient interval rates were lower in the West than in any other region.

Overall, private insurance was the expected primary source of payment for the majority of tubal sterilizations nationwide (58%) and in each region (Table 5,

page 164). Medicaid was the expected primary source of payment for one-third of all sterilizations, with this percentage varying from 19% in the Northeast to 37-39% in the West and South. Among women having a postpartum procedure, private insurance was the expected source of payment for 48% overall, while 41% were paid for through Medicaid. In contrast, private insurance was the expected source of payment for the large majority of outpatient interval sterilization procedures (68%), and Medicaid paid for 24%. In the Northeast, Medicaid was the expected source of payment for a smaller proportion of outpatient interval sterilizations than in any other region.

Fifty-eight percent of women who had a postpartum sterilization had a vaginal delivery, and 42% had a cesarean delivery. Among women obtaining an interval sterilization, laparoscopic procedures were used in 89% of outpatient sterilizations and in 53% of inpatient procedures. For women who underwent tubal sterilization on an outpatient basis, general anesthesia was the method of anesthesia used most frequently (in 93% of procedures), while topical or local anesthesia (2%), regional anesthesia (2%) and methods classified as other (6%) were used rarely. (These percentages exceed 100% when totaled because some records indicate more than one type of anesthesia.) Data on anesthesia were not available from NHDS.

Discussion

In the 1970s, tubal sterilization emerged as one of the most common methods of contraception for women of reproductive age in the United States. Female sterilization rates increased from 4.7 per 100,000 women in 1970 to 12.4 per 100,000 by 1980,⁸ and appear to have remained stable over the next two decades, with the rate for 1994-1996 (11.5 per 100,000) being similar to the rate in 1980.

While all postpartum tubal sterilization procedures continue to be performed in hospitals, there has been a significant change in clinical setting for interval procedures in the past 25 years. Technical advances, particularly the use of the laparoscope, have significantly affected the setting in which tubal sterilization procedures can be performed and the trend toward interval sterilization.⁹ In 1970, fewer than 1% of sterilizations not associated with a delivery were performed on an outpatient basis; by 1980, 19% of women having an interval tubal sterilization did not remain in the hospital overnight. Both the number and rate of interval procedures performed in hospitals decreased beginning in 1980, as more ambulatory procedures were performed in hospitals or in freestanding surgery centers. In 1987, 34% of all tubal sterilizations were performed in outpatient settings;¹⁰ this proportion increased to almost 50% by 1994-1996. Although most interval procedures are performed in outpatient settings, a small proportion of interval procedures are performed on an inpatient basis, most likely for medical indications.

The timing of a sterilization procedure influences the surgical approach. Most

inpatient tubal sterilizations are completed by surgical approaches other than laparoscopy. Postpartum sterilizations are performed at the time of cesarean delivery, when the abdomen is open, or following a vaginal delivery, using a 2-5 cm subumbilical minilaparotomy incision.¹¹ Laparoscopy is not used for postpartum sterilization because the size of the uterus would make insertion of the instrument unsafe. Most interval sterilization procedures in the United States are laparoscopic procedures performed under general anesthesia in an outpatient setting. The proportion of interval procedures performed using laparoscopy increased dramatically between 1970 and 1978 (from fewer than 1% to 51%).¹² Laparoscopy continued to increase in usage, from 79% of outpatient interval sterilizations in 1987¹³ to 89% during the current study period.

Similar to what was seen in previous studies,¹⁴ overall tubal sterilization rates in 1994-1996 were highest among women aged 25-34. The peak childbearing years are 20-29,¹⁵ and most women have had the number of children they desire before age 35. As a result of the cumulative effect of sterilizations over the reproductive age span, 50% of all contraceptive users 40-44 years of age relied on female sterilization in 1995.¹⁶

Tubal sterilization rates among black women were more than twice those of white women in 1970 (9.0 versus 4.1 per 100,000).¹⁷ Although by 1975 tubal sterilization rates had increased twofold among white women and differences by race had narrowed,¹⁸ rates increased more for black women and have remained higher than those for white women since 1976.¹⁹ Our ability to conduct analyses by race in this article was limited because of the high proportion of procedures with unknown race (21-29%), and because hospitalizations in the NHDS for which the patient's race is marked as unknown are not proportionally distributed among all race groups.²⁰ Comparisons of data from the NHDS with data from other sources suggest that race was underreported to a greater extent for white patients than for patients of other races.

While our results must be interpreted with caution, the differences we found between black and white postpartum rates are large enough to remain significant when all women whose race was not stated are added to the white category. This difference by race in some sterilization rates may be explained in part by the fact that non-Hispanic white married or cohabitating women rely on vasectomy as a method of permanent sterilization more frequently (10%) than do black married or cohabitating women (1%).²¹ Women who choose tubal sterilization tend to be less-educated and to have lower levels of income,²² likewise, black women have been shown to have lower levels of income, education and access to health care.²³ These and other factors, rather than race itself, most likely account for differences between black and white women in tubal sterilization rates.

We found that regional differences in overall tubal sterilization rates continued in a pattern similar to those reported for the 1970s and 1980s, with the South having the highest rates.²⁴ Notable in our findings are the higher share of interval versus postpartum procedures in the Northeast and Midwest, compared with an inverse relationship between interval and postpartum rates in the South and West. Although our data do not provide insights into the reasons for regional differences, other researchers have suggested that these may be due in part to variations in physicians' attitudes toward sterilization, in the medical care delivery system and in patients' religious beliefs.²⁵ Offsetting variations in vasectomy rates may also account for regional variations in tubal sterilization rates, although published studies have presented conflicting estimates of regional vasectomy rates.²⁶

Previous studies have not examined the source of payment for tubal sterilizations. We found significant differences by region and timing of procedure in the expected primary source of payment. In all regions, Medicaid was the expected source of payment for a higher proportion of postpartum tubal sterilizations than of outpatient interval sterilizations. This difference is explained by Medicaid restrictions in most states limiting coverage of family planning services, including tubal sterilization, for Medicaid recipients to 60 days postpartum.²⁷ Although nine states had expanded coverage under their Medicaid programs by 1997 to include eligibility for family planning services, in most of these states the expanded coverage was restricted to no more than two years' postpartum for Medicaid recipients or up to two years after loss of regular Medicaid coverage.²⁸ In contrast, women covered by private insurance have greater latitude in choosing the timing of their sterilization, given that tubal sterilization is routinely covered by 85-90% of private health insurance policies.²⁹ In addition, the 30-day waiting period required for federally funded sterilization may adversely affect women covered by Medicaid, compared with women who have private insurance; we cannot measure that impact in this study, however.

Several limitations of this study need to be considered. The estimates of sterilization reported here are lower than the total number of tubal sterilizations in the United States, because our analysis did not include any tubal sterilizations performed in federally operated hospitals and clinics or in family planning clinics. However, in 1987, the Association for Voluntary Surgical Contraception reported that only 2% of all sterilizations were performed in military hospitals and family planning clinics.³⁰

Another shortcoming is that our calculation of tubal sterilization rates includes already-sterile women in the denominator; if women who were already sterile from previous tubal sterilization, from hysterectomy or as a result of other medical conditions were excluded from the denominator, tubal sterilization rates would be higher. Further, the apparent decline in sterilization rates with

increasing age would be less dramatic if rates were based only on women at risk.

Additionally, differences in methodology used to determine outpatient estimates preclude a strict comparison with some previous reports.³¹ Finally, race and ethnicity are not available for all records (as previously discussed), and rates for specific race groups are underestimated to an unknown extent.

A number of factors may affect future trends in sterilization. Recent shifts toward delayed childbearing³² may reduce the number of younger women choosing tubal sterilization. Women marry later and wait longer after marriage to start families.³³ In addition, although early reports suggested an increased risk for cardiovascular disease among oral contraceptive users of older ages, data now support pill use among healthy women older than 35 who do not smoke.³⁴ While overall use of oral contraceptives declined between 1988 and 1995, pill use doubled among women aged 35-39 and rose sixfold among those aged 40-44.³⁵ These factors may increase the age at which a woman considers permanent contraception and the rates at which they choose sterilization.

This study is the first comprehensive analysis of all tubal sterilizations since 1987. Our report updates trends in timing, setting and surgical method of sterilization procedures, and provides information on differences by region and source of payment. The availability of NSAS data from outpatient surgical facilities during 1994-1996 has provided key information for a more complete analysis of tubal sterilization rates in the United States.

While NHDS and NSAS offer the most comprehensive data on tubal sterilizations for 1994-1996, further research would be enhanced by data on patient characteristics not available from these surveys, such as parity, prior method of contraception, marital status and education. In addition, improved reporting of race would allow for an analysis of the interaction of race, region and source of payment.

Currently, national data are not collected annually on procedures performed in hospital ambulatory surgery centers or freestanding surgery centers; NSAS was only conducted during the 1994-1996 time period. Clearly, data on inpatient sterilizations from NHDS, used to determine sterilization estimates in the 1970s and early 1980s, are no longer representative of all sterilizations. Continued surveillance of both inpatient and outpatient procedures is needed to monitor the role of tubal sterilization in contraceptive practice.

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*The "other" category included self-pay, Medicare, other government payments and those marked as "other, specified."

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Deaths attributable to tubal sterilization in the United States, 1977 to 1981

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In 1979, the Centers for Disease Control began surveillance of deaths attributable to tubal sterilization in order to determine why they occur and what may be done to prevent them. Since that time, 29 such deaths have been identified as occurring in the United States from 1977 through 1981. Of these 29 deaths, 11 followed complications of general anesthesia, seven were due to sepsis, four were due to hemorrhage, three were due to myocardial infarction, and four deaths were related to other causes. Some of these deaths might have been prevented by use of endotracheal intubation for general anesthesia, particularly for laparoscopic sterilization, safer use of unipolar coagulation or use of alternative techniques, careful insertion of the needle and trocar for laparoscopy, and discontinuation of oral contraceptives before sterilization. Further surveillance may help to make tubal sterilization even safer. (AM. J. OBSTET. GYNECOL. 146:131, 1983.)

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deaths that occurred in the United States during 1977 to 1981.

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The relationship between induced abortion and outcome of subsequent pregnancies

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We analyzed interview and record review data from 9,823 deliveries to evaluate the relationship between prior history of induced abortion and subsequent late pregnancy outcomes. Complications such as bleeding in the first and third trimesters, abnormal presentations and premature rupture of the membranes, abruptio placentae, fetal distress, low birth weight, short gestation, and major malformations occurred more often among women with a history of two or more induced abortions. A logistic regression analysis to control for multiple confounding factors showed that a history of one induced abortion was statistically significantly associated with first-trimester bleeding but with no other untoward pregnancy events, and a history of two or more induced abortions was statistically associated with first-trimester bleeding, abnormal presentations, and premature rupture of the membranes. While these relationships merit further research, the results of this study are largely reassuring. A history of one or more prior induced abortions does not appear to increase substantially the risk of adverse late outcomes of subsequent pregnancies. (*AM. J. OBSTET. GYNECOL.* 146:136, 1983.)

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Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study

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Despite the contention by some that local anesthesia is a preferred alternative to general anesthesia for laparoscopic sterilization, there have been no randomized studies comparing these techniques. To better characterize the relative safety and acceptability of these techniques for laparoscopic sterilization, we randomly assigned 100 women undergoing bipolar electrocoagulation or spring clip application to either local or general anesthesia. Of the 53 women assigned local anesthesia, four had their procedures completed using another technique because of technical problems related to obesity. Thirteen other obese women, however, underwent successful surgery with local anesthesia. Women undergoing local anesthesia had a slightly shorter anesthesia time (30 versus 36 minutes) and recovery room stay (65 versus 78 minutes). Women having general anesthesia were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate 110 or higher. Patient movement was reported to be a concern in five women undergoing general anesthesia, but in none having local anesthesia. An equal percentage (80%) of women in each group expressed satisfaction with their anesthetic technique. (*Obstet Gynecol* 70:903, 1987)

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The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization

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OBJECTIVE: Our purpose was to determine the risk of pregnancy after tubal sterilization for common methods of tubal occlusion.

STUDY DESIGN: A multicenter, prospective cohort study was conducted in U.S. medical centers. A total of 10,685 women who underwent tubal sterilization was followed up for 8 to 14 years. The risk of pregnancy was assessed by cumulative life-table probabilities and proportional hazards models.

RESULTS: A total of 143 sterilization failures was identified. Cumulative 10-year probabilities of pregnancy were highest after clip sterilization (36.5/1000 procedures) and lowest after unipolar coagulation (7.5/1000) and postpartum partial salpingectomy (7.5/1000). The cumulative risk of pregnancy was highest among women sterilized at a young age with bipolar coagulation (54.3/1000) and clip application (52.1/1000).

CONCLUSIONS: Although tubal sterilization is highly effective, the risk of sterilization failure is higher than generally reported. The risk persists for years after the procedure and varies by method of tubal occlusion and age. (*Am J Obstet Gynecol* 1996;174:1161-70.)

Key words: Tubal sterilization, pregnancy, sterilization failure

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Long-Term Effect of Tubal Sterilization on Menstrual Indices and Pelvic Pain

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Objective: To evaluate the long-term effect of tubal sterilization on menstrual indices and pelvic pain.

Methods: Five hundred women undergoing sterilization were interviewed before sterilization, 6-10 months after surgery, and 3-4.5 years later. Four hundred sixty-six non-sterilized comparison women were interviewed in parallel. The study population consisted of low-income, ethnically and regionally diverse women from three participating institutions.

Results: When women who were taking oral contraceptives were excluded, no long-term difference was found between sterilized and nonsterilized women in terms of menstrual cycles, bleeding between periods, prolonged or heavy flow, dysmenorrhea, or noncyclic pelvic pain. Hysterectomy was uncommon (3.2%), but statistically more prevalent among sterilized women (4.55%) than nonsterilized women (2.17%) ($P = .019$).

Conclusions: Tubal sterilization has no long-term effect on menstrual indices or pelvic pain. An increase in severe dysmenorrhea, which emerged as a disturbing but nonsignificant trend at 6-10 months, did not progress over the next 3-4.5 years. Reasons for an increased rate of hysterectomy are not clear, but may be related to a lower threshold for choosing hysterectomy as a treatment option once a woman has been sterilized. (*Obstet Gynecol* 1993;82:118-21)

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Contraceptive Method Choice in Developing Countries

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CONTEXT: For all persons to enjoy a choice among contraceptive options, a range of methods must be readily available. Yet measures of access show serious deficits that depress use of each method. Countries differ both in the number of methods offered and the extent to which each is made available. Information is needed on how these factors have changed over time and how they have affected contraceptive use overall and use of individual methods.

METHODS: Patterns of contraceptive use are derived from data from national surveys, and levels of access to four methods (female sterilization, the IUD, the pill and the condom) are measured by estimates from cycles of a program effort study of the proportion of couples for whom each method is available, as of 1982, 1989, 1994 and 1999. The analysis focuses on the relationship between access to contraceptives and patterns of use.

RESULTS: In all four cycles of the program effort study, the mean prevalence of the four methods rises with mean access. For example, mean prevalence in 1994 and 1999 was close to 12% in countries with very low access, compared with 44% in those with high access. Prevalence is highest in countries where access to all methods is uniformly high. In 1994, for example, mean prevalence was 12% in countries where mean availability was high and diversity in the availability of individual methods was low, compared with 9% in countries where mean availability was high and access to individual methods varied considerably. Between 1982 and 1994, the number of countries with uniformly high access rose from nine to 23, while the number with uniformly low access declined from 23 to nine. At the lowest level of mean availability, the condom and the pill contribute most to availability (40% and 36%, respectively), but at the highest level, the contributions of the four methods equalize at 22–27% each. The situation for prevalence is similar: The pill's share at the lowest level of availability is 67%, compared with 31% at the highest level, where it is surpassed by female sterilization (36%).

CONCLUSIONS: Full choice among a variety of contraceptive offerings is yet to be attained in many countries. Its absence restricts personal access to each method as well as the use of all methods in the population. To the extent that the ability to choose satisfactory contraceptive protection depends on ready access to multiple methods, a clear mandate exists for greater programmatic attention to the provision of a full range of methods.

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RESUMEN

Contexto: Para que todas las personas puedan disfrutar del uso del anticonceptivo de su elección, se debe tener a disposición una amplia gama de métodos. Todavía las medidas de acceso presentan serias limitaciones que limitan el uso de cada método. Los países difieren tanto con respecto al número de métodos que se ofrecen como la disponibilidad de cada uno. Se necesita información acerca de la forma en que estos factores han cambiado a través del tiempo y sobre la manera en que han afectado el uso de anticonceptivos en general y de algunos en particular.

Métodos: Las pautas de uso de anticonceptivos se determinan en base a los datos obtenidos en las encuestas nacionales y los niveles de acceso a cuatro métodos (esterilización femenina, el DIU, la píldora y el condón) son medidos de acuerdo con el porcentaje estimado de parejas para las cuales cada método se encontraba disponible en 1982, 1989, 1994 y 1999. El análisis se centra en la relación que existe entre el acceso a los anticonceptivos y las pautas de uso.

Resultados: En los cuatro ciclos del estudio de esfuerzo del programa, la prevalencia media de los cuatro métodos aumenta de acuerdo con el promedio de acceso. Por ejemplo, la prevalencia media en 1994 y 1999 fue de cerca del 12% en los países donde el acceso era muy bajo, en comparación con el 44% en aquellos que ofrecían un acceso elevado. La prevalencia presentó su más alto nivel en los países donde el acceso a todos los métodos era uniformemente elevado. En 1994, por ejemplo, la prevalencia media fue del 12% en países donde la disponibilidad media era elevada pero la diversidad en la disponibilidad de determinados métodos era baja, en comparación con una prevalencia del 9% en los países donde la disponibilidad media era elevada y el acceso a determinados métodos variaba considerablemente. Entre 1982 y 1994, el número de países con un acceso elevado uniforme aumentó de nueve a 23, en tanto que el número con acceso uniformemente bajo disminuyó de 23 a nueve. En los más bajos niveles de disponibilidad media, el condón y la píldora contribuyeron en mayor medida a la disponibilidad (40% y 36%, respectivamente), aunque al más elevado nivel, las contribuciones de los cuatro métodos se igualaron en 22-27% cada uno. La situación con respecto a la prevalencia es similar: el porcentaje que le corresponde a la píldora al más bajo nivel es del 67%, en comparación con el 31% al más alto nivel, donde lo supera la esterilización femenina (36%).

Conclusiones: En muchos países aún no se ha logrado disponer de una amplia gama de anticonceptivos. Esta carencia restringe el acceso personal a cada método, así como el uso de anticonceptivos en general. Hasta el punto que la posibilidad de optar por una protección anticonceptiva satisfactoria depende del fácil acceso a métodos múltiples, existe un claro mandato de prestar una mayor atención programática a contar con una amplia gama de métodos.

RÉSUMÉ

Contexte: Pour que chacun puisse bénéficier d'un choix d'options contraceptives, une gamme de méthodes doit être aisément accessible. Les mesures d'accès démontrent cependant de graves lacunes, au détriment de la pratique de chaque méthode. Le nombre de méthodes proposées et la mesure de leur disponibi-

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lité différent d'un pays à l'autre. L'évolution de ces facteurs au fil du temps et leurs effets sur la contraception en général et sur la pratique de méthodes individuelles doivent être documentés.

Méthodes: Les tendances de la pratique contraceptive sont dérivées des données d'enquêtes nationales, et les niveaux d'accès à quatre méthodes (la stérilisation féminine, le stérilet, la pilule et le préservatif) sont mesurés par estimation de la proportion des couples pour lesquels chaque méthode est disponible, à compter de 1982, 1989, 1994 et 1999. L'analyse se concentre sur le rapport entre l'accès aux contraceptifs et les tendances d'usage.

Résultats: Aux quatre cycles de l'étude d'effort programmatique, la prévalence moyenne des quatre méthodes augmente en même temps que l'accès moyen. Ainsi, la prévalence, en 1994 et 1999, était proche de 12% dans les pays caractérisés par un accès très limité, par rapport à 44% dans ceux offrant un accès très élevé. La prévalence atteint les plus haut niveaux dans les pays où l'accès à toutes les méthodes est uniformément élevé. En 1994, par exemple, la prévalence moyenne était de 12% dans les pays à disponibilité moyenne élevée et faible diversité de méthodes individuelles, par rapport à 9% dans ceux où la disponibilité moyenne était élevée mais où l'accès aux méthodes individuelles était largement variable. Entre 1982 et 1994, le nombre de pays offrant un accès uniformément élevé est passé de neuf à 23, tandis que le nombre de ceux présentant un accès

uniformément faible baissait, de 23 à neuf. Au plus faible niveau de disponibilité moyenne, le préservatif et la pilule contribuent le plus à la disponibilité (40% et 36%, respectivement), mais au niveau supérieur, la contribution des quatre méthodes s'égalise, entre 22 et 27% chacune. On observe une situation semblable pour la prévalence: la part de la pilule au plus faible niveau de disponibilité est de 67%, par rapport à 31% au plus haut niveau, où la stérilisation féminine la surpasse (36%).

Conclusions: L'offre d'un choix complet de contraceptifs variés n'est pas encore atteinte dans de nombreux pays. Cette absence limite l'accès personnel à chaque méthode aussi bien que la pratique globale des méthodes au sein de la population. Dans la mesure où la capacité de choisir une protection contraceptive satisfaisante dépend d'un accès aisé à une multiplicité de méthodes, les programmes se doivent clairement d'accorder une plus grande attention à la fourniture d'une gamme complète de méthodes.

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The legal status of abortion varies widely around the world, but health care providers in all countries share a need for information on treatment for complications from spontaneous or induced abortion. In response to this need, the September 2003 issue of *International Family Planning Perspectives* will include a special section on postabortion care as part of the journal's "Issues in Perspective" series. We are seeking papers on provision of postabortion care; integration of family planning counseling and services with postabortion care; the technology, training and costs involved in initiating services; quality of care; and access issues. We will consider commentaries as well as qualitative and quantitative research.

To be eligible for the special section, papers should be no more than 3,000 words and must be received by November 1, 2002. Authors should follow the journal's style, as detailed in the Guidelines for Authors, which can be found in this issue and on our Web site, www.guttmacher.org/guidelines.

Please send submissions to Patricia Donovan, Editor in Chief, *International Family Planning Perspectives*, The Alan Guttmacher Institute, 120 Wall Street, New York, NY 10005. Questions about the special section should be addressed to Patricia Donovan at pdonovan@guttmacher.org.

Deadline: November 1, 2002

Two randomized controlled trials comparing the Tubal Ring and Filshie Clip for tubal sterilization

David Sokal, M.D., Deborah Gates, M.P.H., Ramesh Amatya, Ph.D.,
Rosalie Dominik, M.P.H., and the Clinical Investigator Team

Family Health International, Research Triangle Park, North Carolina

Objective: To compare the effectiveness and safety of the Filshie Clip and Tubal Ring systems when applied via minilaparotomy and laparoscopy.

Design: Prospective, multicenter randomized controlled clinical trial, with postoperative evaluation by a physician who was masked to the operative technique.

Setting: Healthy volunteers in a variety of hospital settings.

Patient(s): 2746 women (915 in the minilaparotomy study and 1831 in the laparoscopy study) who had requested permanent surgical sterilization.

Intervention(s): Surgical tubal ligation, using either Filshie Clips or Tubal Rings. A physician other than the surgeon evaluated the patients after the operation and again at 1, 6, and 12 months after surgery.

Main Outcome Measure(s): Pregnancy rates and safety-related events.

Result(s): During the 12 months after surgery, two women who received the Filshie Clip and two women who received the Tubal Ring became pregnant, giving a 12-month life-table pregnancy probability of 1.7 per 1000 women in both groups. The Tubal Ring was more difficult to apply and had higher rates of tubal or mesosalpingeal injuries at surgery. The Filshie Clip group had three cases of spontaneous clip expulsion during the follow-up period.

Conclusion(s): Both the Filshie Clip and Tubal Ring are effective and safe for use in tubal occlusion. (*Fertil Steril*® 2000;74:525-33. ©2000 by American Society for Reproductive Medicine.)

Key Words: Tubal occlusion devices, female sterilization, Filshie Clip, Tubal Ring

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Reprint requests: David Sokal, P.O. Box 13950, Family Health International, Research Triangle Park, North Carolina 27513 (FAX: 919-544-7261; E-mail: dsokal@fhi.org).

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Contraceptive Failure, Method-Related Discontinuation And Resumption of Use: Results from the 1995 National Survey of Family Growth

By James Trussell and Barbara Vaughan

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Context: *Half of all pregnancies in the United States are unintended. Of these, half occur to women who were practicing contraception in the month they conceived, and others occur when couples stop use because they find their method difficult or inconvenient to use.*

Methods: *Data from the 1995 National Survey of Family Growth were used to compute life-table probabilities of contraceptive failure for reversible methods of contraception, discontinuation of use for a method-related reason and resumption of contraceptive use.*

Results: *Within one year of starting to use a reversible method of contraception, 9% of women experience a contraceptive failure—7% of those using the pill, 9% of those relying on the male condom and 19% of those practicing withdrawal. During a lifetime of use of reversible methods, the typical woman will experience 1.8 contraceptive failures. Overall, 31% of women discontinue use of a reversible contraceptive for a method-related reason within six months of starting use, and 44% do so within 12 months; however, 68% resume use of a method within one month and 76% do so within three months. Multivariate analyses show that the risk of contraceptive failure is elevated among low-income women and Hispanic women. Low-income women are also less likely than other women to resume contraceptive use after discontinuation.*

Conclusions: *The risks of pregnancy during typical use of reversible methods of contraception are considerably higher than risks of failure during clinical trials, reflecting imperfect use of these methods rather than lack of inherent efficacy. High rates of method-related discontinuation probably reflect dissatisfaction with available methods.*

Family Planning Perspectives, 1999, 31(2):64-72 & 93

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BRIEF REPORT

Natural Limits of Pregnancy Testing in Relation to the Expected Menstrual Period

Allen J. Wilcox, MD, PhD

Donna Day Baird, PhD

David Dunson, PhD

Ruth McChesney, PhD

Clarice R. Weinberg, PhD

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Context Pregnancy test kits routinely recommend testing "as early as the first day of the missed period." However, a pregnancy cannot be detected before the blastocyst implants. Due to natural variability in the timing of ovulation, implantation does not necessarily occur before the expected onset of next menses.

Objective To estimate the maximum screening sensitivity of pregnancy tests when used on the first day of the expected period, taking into account the natural variability of ovulation and implantation.

Design and Setting Community-based prospective cohort study conducted in North Carolina between 1982 and 1986.

Participants Two hundred twenty-one healthy women 21 to 42 years of age who were planning to conceive.

Main Outcome Measures Day of implantation, defined by the serial assay of first morning urine samples using an extremely sensitive immunoradiometric assay for human chorionic gonadotropin (hCG), relative to the first day of the missed period, defined as the day on which women expected their next menses to begin, based on self-reported usual cycle length.

Results Data were available for 136 clinical pregnancies conceived during the study, 14 (10%) of which had not yet implanted by the first day of the missed period. The highest possible screening sensitivity for an hCG-based pregnancy test therefore is estimated to be 90% (95% confidence interval [CI], 84%-94%) on the first day of the missed period. By 1 week after the first day of the missed period, the highest possible screening sensitivity is estimated to be 97% (95% CI, 94%-99%).

Conclusions In this study, using an extremely sensitive assay for hCG, 10% of clinical pregnancies were undetectable on the first day of missed menses. In practice, an even larger percentage of clinical pregnancies may be undetected by current test kits on this day, given their reported assay properties and other practical limitations.

JAMA. 2001;286:1759-1761

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Menstrual Function after Tubal Sterilization

Lynne S. Wilcox,¹ Beverly Martinez-Schnell,¹ Herbert B. Peterson,¹ James H. Ware,² and Joyce M. Hughes¹

More than 10 million women in the United States have undergone tubal sterilization. There has been concern that this procedure may increase the risk of later menstrual dysfunction. The Collaborative Review of Sterilization (CREST) is a large, multicenter, prospective study of tubal sterilization in the United States. This report describes CREST participants who were interviewed immediately before sterilization and again in annual poststerilization interviews for up to 5 years between 1978 and 1988. The authors analyzed reported changes in six menstrual cycle characteristics for 5,070 women undergoing interval sterilizations. Longitudinal, multivariate regression was used to adjust for baseline menstrual function and other potential confounders. Five years after sterilization, 35% of the CREST participants reported high levels of menstrual pain, 49% reported heavy or very heavy menstrual flow, and 10% reported spotting between periods. In contrast to the fifth year, the first year of follow-up was similar to presterilization menstrual function; in the first year, 27% of participants reported high menstrual pain, 41% reported heavy menstrual flow, and 7% reported spotting. These findings may be affected by aging of the cohort and other study limitations, but they suggest that if tubal sterilization leads to changes in menstrual function, such changes may take some time to develop. *Am J Epidemiol* 1992;135:1368-81.

menstruation; menstruation disorders; sterilization, tubal

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Received for publication March 4, 1991, and in final form December 6, 1991.

Abbreviation: CREST, Collaborative Review of Sterilization.

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Reprint requests to Dr. Lynne S. Wilcox, Women's Health and Fertility Branch, Division of Reproductive Health, Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control, 1600 Clifton Road N. E., Mailstop K34, Atlanta, GA 30333.

The Collaborative Review of Sterilization was supported in part by an interagency agreement between the Centers for Disease Control and the National Institute of Child Health and Human Development (Y01-HD-41075), Bethesda, MD.

The Collaborative Review of Sterilization—Design, Coordination, and Analysis Center: Women's Health and Fertility Branch, Division of Reproductive Health, Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control, Atlanta, GA. Data Collection Centers Project Directors: Dr. Norman Courey, Erie County Research for Health, Buffalo, NY; Dr. Ernst Friedrich, Washington University School of Medicine, St. Louis, MO; Dr. J. F. Hulka, University of North Carolina School of Medicine, Chapel Hill, NC; Dr. Ralph W. Hale, Kapiolani Medical Center, Honolulu, HI; Dr. Gary Stewart, Planned Parenthood of Sacramento, Sacramento, CA; and Dr. Howard A. Zacur, The Johns Hopkins University School of Medicine, Baltimore, MD.

The authors gratefully acknowledge Dr. Scott Zeger, who shared his generalized estimating equations software with them.

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June 12, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Amendment #2 to PMA No. P020014
Revised Instructions for Use and Summary of Safety and Effectiveness
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6)

Conceptus is submitting this PMA amendment to provide the Agency with a revised Instructions for Use (IFU) and a revised Summary of Safety and Effectiveness (SS&E). Both documents have been revised (as shown below) to incorporate the changes requested by (b) (6) on June 11, 2002. Additionally, the Device Description section of the Summary of Safety and Effectiveness has been revised to be consistent with the Device Description section included in the Instructions for Use. No other changes have been made.

RECEIVED
JUN 13 11 41 AM '02
FDA/CDRH/DOE/MSD

IFU Revisions

- Page 6 - Added "in women relying on Essure" to end of first bullet point.
- Pages 6 and 8 - The year in the footnote has been changed from 1988 to 1998.

SS&E Revisions

- Page 9 - Added "in women relying on Essure" to end of first bullet point.
- Pages 1 - 4 - Revised Device Description section to be consistent with Device Description section included in the IFU.

If you have any questions regarding this amendment, I can be reached at (b) (6) or by fax at (b) (6) or by e-mail at (b) (6). In addition, you may contact Susan Aloyan at (b) (6) by fax at (b) (6) or by e-mail at (b) (6). Thank you for your continued review of this PMA application.

Sincerely,

(b) (6)

[Redacted signature block]

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Food and Drug Administration
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Re: Amendment to PMA No. P020014
Formal Amendment to respond to (b) (6) question on Platinum Leaching
Rate (email dated 9/20/02)
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6):

Conceptus Inc. is submitting this PMA Amendment to formalize its response to (b) (6) question (email dated 9/20/02) concerning Platinum leaching rate (Question #1). This response was provided to (b) (6) via email on September 20, 2002.

Below is a brief summary of the communication in this regard:

Summary

- September 19, 2002 – (b) (6) questions received regarding “Essure Corrosion and Shelf Life” (e-mail)
- September 20, 2002 – PMA Amendment responding to questions of 9/19/02 submitted (letter and email)


(b) (6), (b) (4)



SP4

Conceptus, Inc.

(b) (6), (b) (4)



Please note that this Amendment does not alter any information communicated previously by email. This letter only acts as a formal Amendment.

If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)



2

P020014

A6

C15

Conceptus_o

June 22, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Amendment to PMA No. P020014
Response to Agency Request for Articles on Ovabloc and Femcept Device
Conceptus EssureTM System for Permanent Birth Control

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Dear (b) (6)

The Agency requested that we supply a copy of published articles regarding the Ovabloc (silicone plug) and Femcept (methylcyanoacrylate) tubal occlusion devices. A literature search was conducted and the publication lists are provided in Attachment A and B, respectively. A copy of each of the articles referenced follows each respective list, with the exception of two articles on Ovabloc, which we have ordered from foreign journals but have not yet been received (#4, van der Leij and #7, Loffer). We will supply these articles once received.

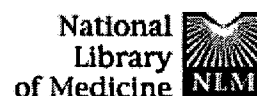
In addition, although not requested, we can supply copies of articles for the following tubal occlusion devices, which have been tested clinically by other researchers: P-block (Hydrogel-nylon), Hamou Plug (Nylon), and the Hosseinian UTJ device (Polymer-Elgiloy). Please let us know if the Agency would like this additional information to be submitted.

If you have any questions, I can be reached at (b) (6) or by fax at (b) (6)
(b) (6) or by e-mail at (b) (6)

Sincerely,

(b) (6)

Enclosures: Attachment A and B (2 copies)



PubMed Nucleotide Protein Genome Structure PopSet Taxonomy OMIM Bc

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- 1: Ligt-Veneman NG, Tinga DJ, Kragt H, Brandsma G, van der Leij G.** Related Articles
 The efficacy of intratubal silicone in the Ovabloc hysteroscopic method of sterilization.
 Acta Obstet Gynecol Scand. 1999 Oct;78(9):824-5. No abstract available.
 PMID: 10535350 [PubMed - indexed for MEDLINE]
- 2: van der Leij G, Lammes FB.** Related Articles
 Radiographic aspects of office hysteroscopic tubal occlusion with siloxane intratubal devices (the Ovabloc method).
 Int J Gynaecol Obstet. 1997 Nov;59(2):123-31.
 PMID: 9431875 [PubMed - indexed for MEDLINE]
- 3: van der Leij G, Lammes FB.** Related Articles
 Office hysteroscopic tubal occlusion with siloxane intratubal devices (the Ovabloc method).
 Int J Gynaecol Obstet. 1996 Jun;53(3):253-60.
 PMID: 8793628 [PubMed - indexed for MEDLINE]
- 4: van der Leij G, van Krimpen C.** Related Articles
 Impact of Ovabloc intratubal polymer on the morphology of the fallopian tube.
 Int J Gynecol Pathol. 1995 Apr;14(2):167-73.
 PMID: 8601529 [PubMed - indexed for MEDLINE]
- 5: Huvar I, Tinga D, Pilka L.** Related Articles
 [Hysteroscopic sterilization using Ovabloc]
 Ceska Gynekol. 1994 Aug;59(4):193-5. Czech.
 PMID: 7812589 [PubMed - indexed for MEDLINE]
- 6: Assaf A, Abdin F, Elkady A, Gohar M, Abd AlAziz A, Abd Alhady M.** Related Articles
 Histopathological effects of silicone rubber 'Ovabloc' on the human fallopian tube.
 Int J Gynaecol Obstet. 1993 Nov;43(2):181-9.
 PMID: 7905435 [PubMed - indexed for MEDLINE]
- 7: Loffer FD, Loffer PS.** Related Articles
 Learning hysteroscopy sterilization and the Ovabloc System with Hyskon.
 Acta Eur Fertil. 1986 Nov-Dec;17(6):477-80.
 PMID: 3630560 [PubMed - indexed for MEDLINE]

8:Reed TP 3rd.

Related Articles

Ovabloc. Five years of experience.
J Reprod Med. 1984 Aug;29(8):601-2.
PMID: 6481715 [PubMed - indexed for MEDLINE]

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Acta Obstetrica et
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SHORT REPORT

The efficacy of intratubal silicone in the Ovabloc hysteroscopic method of sterilization

NETTY G. P. LIGT-VENEMAN¹, DICK J. TINGA¹, HARRY KRAGT², GIRBE BRANDSMA² AND GERARD VAN DER LEIJ³

From the Departments of Obstetrics and Gynecology, ¹the University Hospital, Groningen, ²the Diaconessen Hospital, Voorburg, and ³the Schiealand Hospital, Schiedam, The Netherlands

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Key words: hysteroscopy; Ovabloc; pregnancy-rate; silicone; sterilization

Submitted 18 February, 1999

Accepted 26 April, 1999

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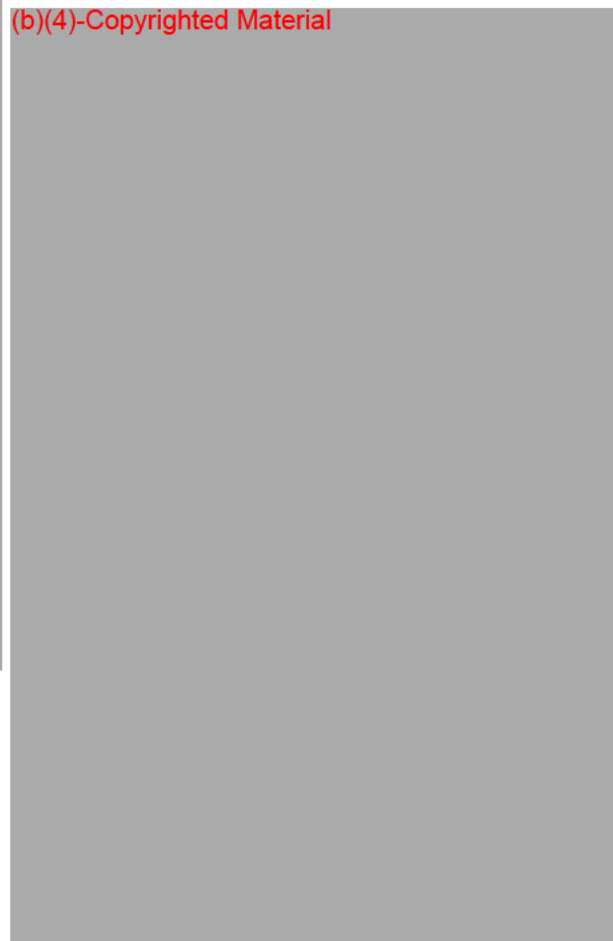


Table I. Efficacy criteria for Ovabloc*

Successful instillations	325 (100%)
Successful instillation rate (3 months)	314 (96.6%)
Successful instillation rate (1 year)	306 (93.8%)
Pregnancy rate	0.99%
Continuation rate	90.2%

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International Journal of
**GYNECOLOGY
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International Journal of Gynecology & Obstetrics 59 (1997) 123-131

Article

**Radiographic aspects of office hysteroscopic tubal
occlusion with siloxane intratubal devices
(the Ovabloc® method)**

G. van der Leij^{a,*}, F.B. Lammes^b

^aDepartment of Obstetrics and Gynaecology, Schieland Hospital, Schiedam, The Netherlands

^bDepartment of Gynaecology, Academic Medical Centre, Amsterdam, The Netherlands

Received 29 May 1997; accepted 28 July 1997

Abstract

Objective: To evaluate the importance of radiographs in women sterilized with hysteroscopically applied siloxane intratubal devices (ITDs). **Methods:** A retrospective study of the frequency of abnormal radiographs in 500 women was carried out. The agreement in judging these radiographs and the expected reliability of the sterilization was measured. **Results:** Abnormal radiographs were mostly documented in the first 100 sterilization procedures. Agreement in judging the radiographs is substantial. Different agreements on the expected reliability are due to the difference in experience with this sterilization method. **Conclusions:** Four types of abnormal radiographs can be categorized. Judgment of the radiographs can easily be learned. For the assessment of the reliability, training is necessary. © 1997 International Federation of Gynecology and Obstetrics

Keywords: Female sterilization; Ovabloc®; Intratubal devices; Hysteroscopy

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International Journal of Gynecology & Obstetrics 53 (1996) 253-260

Article

Office hysteroscopic tubal occlusion with siloxane intratubal devices (The Ovabloc® method)

G. van der Leij^a, F.B. Lammes^b

^aDepartment of Obstetrics and Gynaecology, Schieland Hospital, Schiedam, The Netherlands

^bDepartment of Gynaecology, Academic Medical Centre, Amsterdam, The Netherlands

Received 12 September 1995; revised 10 January 1996; accepted 22 January 1996

Abstract

Objectives: To study the results of the Ovabloc® method for female sterilization used in an outpatient setting. **Methods:** A prospective longitudinal study at the Schieland Hospital of 411 patients who consented for the method for sterilization. For statistical analyses the χ^2 test is used for detection of differences between groups of patients. The life-table analysis is used for events during the follow-up period. **Results:** Our results reflect those done under strict clinical conditions. The majority of the events took place in the first 36 months on Ovabloc®. Unplanned pregnancies were mainly due to misdiagnosis in X-ray images and to incomplete procedures. **Conclusions:** The method failures are 3/1000 women in 12 months and 8/1000 women in 36 months. The follow-up should be extended to 12 months. The reversibility of the method remains questionable. The method should be offered to women with (relative) contraindications for laparoscopic sterilization such as severe obesity, extensive pelvic adhesions or anesthetic risks.

Keywords: Hysteroscopy; Ovabloc®; Female sterilization; Siloxane rubber

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Prof. MUDr. J. Kocián, DrSc.
I. interní klinika IPVZ - FTN
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Hysteroskopická sterilizace Ovablokem

Čes. Gynec.
59, 1994, č. 4
s. 193 - 195

Hysteroscopic Sterilization by Ovabloc

I. Huvar, D. Tinga, L. Pilka

II. gynec. porod. klinika LF MU, Brno, přednostka prof. MUDr. L. Pilka, DrSc.
Afdeling Obstetrie en Gynaecologie A.Z.G., Groningen, přednostka prof. Dr. J. Aalders

S u m m a r y: The authors give an account on 29 sterilizations made by the hysteroscopic route, using the preparation OVABLOC. It is a reversible block of the oviducts by occlusive material. Under hysteroscopic control into the inner orifice of the oviduct by means of a special injecting device under pressure a two-component mixture of silicone and a catalyst is installed which causes within 5 min. hardening of the mass and the formation of an elastic relief filling of the entire oviduct. In 25 of the women (86.2%) the procedure was accomplished without complication, in the 3 (10.3%) the procedure failed on account of technical difficulties and in one case (3.3%) during hysteroscopy the uterine wall was perforated. On X-ray check-up after three months of 25

successfully operated women in 24 the position of the tubal occlusion was unaltered (the material is due to dispersed silver particles contrasting on X-ray); in one case it was loosened. The advantages of the method are that it is sparing, well tolerated and easily reversible, the disadvantage is that it is relatively laborious and expensive.

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Histopathological effects of silicone rubber 'Ovabloc' on the human fallopian tube

A. Assaf^a, F. Abdin^b, A. Elkady^c, M. Gohar^a, A. Abd AlAziz^a and M. Abd Alhady^a

^aDepartment of Gynecology and Obstetrics, Benha University Hospital, ^bDepartment of Histopathology, Al-Azhar University Hospital and ^cDepartment of Gynecology and Obstetrics, Boulak E. Dakrou Hospital (Egypt)

(Received January 25th, 1993)
(Revised and accepted June 6th, 1993)

Abstract

OBJECTIVE: To study the histopathological effects of silicone rubber on the human fallopian tube. **METHODS:** A prospective longitudinal study at Benha University Hospital and Boulak Eldakrou General Hospital, Egypt. Nine patients who were on the waiting list for hysterectomy and requested postponing of their operation for personal reasons. **RESULTS:** Our results suggest that silicone rubber induces histopathological changes in the form of ciliary loss and intracellular changes. **CONCLUSIONS:** These effects tend to increase with the increase of the duration of tubal plugging and are best seen by electron microscopy.

Keywords: Silicone rubber; Hysterectomy; Female sterilization; Histopathology.

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Ovabloc
Five Years of Experience

Theodore P. Reed III, M.D.

Female sterilization with the Ovabloc was performed on 438 women in five years. The complications, failure rate and pregnancy rate are discussed.

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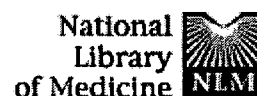


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Update on transcervical sterilization

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Abstract

Transcervical sterilization techniques as of 1980 are reviewed. A personal and literature search is reported on developments between 1980 and 1992. The potential of endometrial ablation for a transcervical method of fertility control is explored. An appraisal of the more promising methods for future study is made, including silastic tubal plugs, quinacrine, Femcept delivery of an iodine mixture and endometrial ablation.

Keywords: Transvaginal sterilization; Transcervical sterilization

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TRANSACTIONS OF THE FORTY-FOURTH ANNUAL MEETING OF THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Transcervical sterilization with use of methyl 2-cyanoacrylate and a newer delivery system (the FEMCEPT device)

Jack Shuber, MD

Toronto, Ontario, Canada

The increasing use of sterilization as a means of permanent contraception prompts the search for simpler, safer methods. Methyl 2-cyanoacrylate 0.6 ml was administered to the uterocornual tubal junction with the use of the FEMCEPT transcervical delivery system in 35 healthy parous women aged 30 to 44 years. Hysterosalpingography 4 months after the procedure showed bilateral tubal occlusion in 88.2% of the study participants. There were no complications in the study group, and there were no pregnancies among those who demonstrated bilateral tubal occlusion. The technique, which is safe, effective, and simple, could considerably reduce anesthetic and operative risk in sterilization. (*Am J Obstet Gynecol* 1989;160:887-9.)

Key words: Sterilization, transcervical, methyl 2-cyanoacrylate, FEMCEPT

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The Incidence of Asymptomatic Uterine Anomalies in Women Undergoing Transcervical Tubal Sterilization

D. ASHTON, MD, H. K. AMIN, MD, R. M. RICHART, MD, AND
R. S. NEUWIRTH, MD

The incidence of congenital anomalies of the uterus has generally been obtained from studies of women undergoing evaluation for infertility, and has been reported as 1-10%. However, the true incidence of uterine malformations is not known. This study reviews hysterosalpingograms obtained for evaluation of tubal closure after transcervical sterilization in normal multiparous women using methylcyanoacrylate and the FEMCEPT device. Of the 840 hysterosalpingograms studied, 16 congenital uterine anomalies were identified, for an incidence of 1.9%. The presence of anomalies in this population of women may more closely represent the incidence of congenital uterine anomalies in the general population. (*Obstet Gynecol* 72:28, 1988)

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Intrauterine administration of methyl cyanoacrylate as an outpatient method of permanent female sterilization

Ralph M. Richart, M.D., Robert S. Neuwirth, M.D., Alfredo Goldsmith, M.D., M.P.H., and David A. Edelman, Ph.D.

New York, New York, Chicago, Illinois, and Chapel Hill, North Carolina

Results are presented of multicenter studies on the intrauterine delivery of 0.6 ml methyl cyanoacrylate with the FEMCEPT device (BioNexus Inc., Raleigh, North Carolina) for the purpose of causing permanent obstruction of the fallopian tubes. The studies included 1279 women and were conducted under several different protocols that required either one or two methyl cyanoacrylate application procedures. Based on hysterosalpingograms obtained about 16 weeks after the last methyl cyanoacrylate application, one procedure resulted in a tubal closure rate of 71.4% and two procedures resulted in a tubal closure rate of 89.4%. Complications of the procedure were infrequent and none required surgical treatment. Cumulative pregnancy rates among women with hysterosalpingogram-demonstrated bilateral tubal closure were similar for the one- and two-application procedures that used nonradiopaque methyl cyanoacrylate and were significantly lower ($p < 0.05$) compared with a single application of radiopaque methyl cyanoacrylate. The 3-year pregnancy rate for two applications of nonradiopaque methyl cyanoacrylate was 1.7 ± 1.2 per 100 women. (AM J OBSTET GYNECOL 1987;156:981-7.)

Key words: Methyl cyanoacrylate, tubal occlusion, fallopian tube, hysterosalpingogram



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OCCLUSION TUBARIA NO QUIRURGICA: USO DEL METILCIANOACRILATO (MCA) Y EL DISPOSITIVO FEMCEPT

VICENTE DÍAZ-SÁNCHEZ*, M. C. ONEGA*, FRANCISCO QUIROZ**,
MARIO DOMENZÁIN*, EARLE WILSON*** Y G. PÉREZ-PALACIOS*

En un estudio clínico de fase II se determinó en 26 mujeres voluntarias la efectividad y seguridad de un método para producir oclusión tubaria no quirúrgica. El procedimiento empleado consistió en la aplicación única de Metilcianoacrilato (MCA) a través del cuello uterino usando el dispositivo FEMCEPT. En todos los casos la maniobra se efectuó sin complicaciones. La efectividad del método fue evaluada por medio de Histerosalpingografía practicada 16 semanas después de la instilación del agente químico. En el 72% de los sujetos (18) se demostró la oclusión tubaria bilateral, en el 28% (7) hubo falla del método, y en el 3.3% (1) no se documentó.

A tres años de seguimiento clínico no han ocurrido embarazos en los casos donde se documentó oclusión tubaria bilateral.

Se demuestra que es posible ofrecer a la mujer que desea un método anticonceptivo definitivo una técnica simple, segura y efectiva que no requiere internamiento hospitalario, medicación anestésica ni la invasión de la cavidad abdominal.

NON-SURGICAL TUBAL OCCLUSION. USE OF METHYLCIANOACRILATE THROUGH A BLIND DELIVERY SYSTEM (FEMCEPT)

Sterilization is a highly means of fertility regulation and ranks as the most popular method worldwide. A procedure is needed that can be performed without surgical entry of the woman's abdominal cavity, and is safe, effective, simple in design and easy to learn. A limited Phase II multicentre trial was promoted by the World Health Organization to determine the efficacy and safety of the use of a blind delivery system (Femcept) by trained medical personnel to instill a chemical occlusive agent (Methylcianoacrilate) into the fallopian tubes to produce permanent sterilization. The Family Planning Clinic of the Department of Reproductive Biology at the Instituto Nacional de la Nutrición Salvador Zubirán, conducted the study in 26 volunteer healthy women asking for a permanent method of fertility control. The subjects were between 25 and 40 years of age. The procedure was performed fully ambulatory in all cases. Steroid contraceptive methods were provided until bilateral tubal occlusion was documented. Bilateral tubal occlusion was demonstrated in 18 cases (72%). The overall method's failure was 28% (7 cases of tubal patency and one case of lost of follow-up). At three years no pregnancies have been reported. The method was simple and safe, however efficacy must be increased to be an alternative choice to the current surgical procedures.

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Trials with the FEMCEPT method of female sterilization and experience with radiopaque methylcyanoacrylate

ROBERT S. NEUWIRTH, M.D.

RALPH M. RICHART, M.D.

LEE R. BOLDUC, B.M.E.

ROBERT E. KRALL, Ph.D.

New York, New York, and Raleigh, North Carolina

A previous report described the development of a blind method to deliver methylcyanoacrylate (MCA) transcervically. Using 0.6 ml of a stable MCA whose polymerization time was closely controlled, we reported a 78% bilateral tubal closure rate in 23 cases with hysterosalpingographic control. Subsequent to the previous report, we initiated a study in which patients were randomly assigned to one of three treatment groups: a single MCA injection, a single MCA injection after uterine lavage, or two MCA injections 1 month apart. In addition, a radiopaque MCA has been developed with which it is possible to determine tubal entry after its application by means of the FEMCEPT device. Patients treated with radiopaque MCA have been studied to determine whether it is possible to predict tubal closure on the basis of tubal entry and distribution patterns. The results of these studies and their implications for contraceptive effectiveness of the FEMCEPT/MCA system will be reported. (AM. J. OBSTET. GYNECOL. 145:948, 1983.)

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From the Department of Obstetrics and Gynecology, Woman's Hospital, St. Luke's-Roosevelt Hospital Center, the Department of Pathology, The Sloane Hospital for Women, Columbia-Presbyterian Medical Center, and BioNexus, Inc.

This project was funded by Program for Applied Research on Fertility Regulation (PARFR) Contract No. 240, Northwestern University, supported by the Agency for International Development.

Presented by invitation at the First Annual Meeting of the American Gynecological and Obstetrical Society, Hot Springs, Virginia, September 8-11, 1982.

Reprint requests: Robert S. Neuwirth, M.D., Department of Obstetrics and Gynecology, St. Luke's-Roosevelt Hospital Center, New York, New York 10025.

REFERENCES

1. Richart, R. M., Neuwirth, R. S., and Taylor, H. C., Jr.: Experimental studies of fallopian tube blockade in human sterilization, Springfield, Illinois, 1972, Charles C Thomas, Publisher.
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3. Neuwirth, R. S., Richart, R. M., Stevenson, T. C., B. L. R., Zinser, H., Baur, H., Cohen, J., Elderin-Argueta-Rivas, G., and Nilsen, P. A.: An outpatient approach to female sterilization with methylcyanoacrylate. *AM. J. OBSTET. GYNECOL.* **136**:951, 1980.

Editors' note: This manuscript was revised after these discussions were presented.

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REFERENCE

1. McCausland, A. M.: Endosalpingosis ("endosalpingo-blastosis") following laparoscopic tubal coagulation as an etiologic factor of ectopic pregnancy, *AM. J. OBSTET. GYNECOL.* **143**:12, 1982.

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An outpatient approach to female sterilization with methylcyanoacrylate

ROBERT S. NEUWIRTH, M.D.
RALPH M. RICHART, M.D.
THOMAS STEVENSON, M.D.
LEE R. BOLDUC, M.E.
HANS ZINSER, M.D.
HANS BAUR, M.D.
JEAN COHEN, M.D.
GERD ELDERING, M.D.
GASTAVO ARGUETA RIVAS, M.D.
PER AGNAR NILSEN, M.D.
New York, New York

MCA is a tissue adhesive which can be delivered transcervically to the Fallopian tubes by means of the FEMCEPT device. In the patients treated with this system, both prior to hysterectomy and on an ambulatory basis, there have been no significant complications or side effects. In the most recent series of ambulatory patients treated with the FEMCEPT-MCA system, the bilateral tubal closure rate was 78%. (AM. J. OBSTET. GYNECOL. 136:951, 1960.)

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From St. Luke's Hospital Medical Center, New York; Columbia-Presbyterian Medical Center, New York; The Bolton District General Hospital, Bolton, England; Population Research, Inc., Clearwater, Florida; Evangelische Krankenhaus, Cologne, West Germany; Clinique Maignan, Paris, France; Asociación Dermografica Salvadoreña, San Salvador, El Salvador; Aker Sykehus, Oslo, Norway.

Supported in part by the Program for Applied Research in Fertility Regulation Subcontract No. 86N, AID/csd-3608, "Phase I Clinical Trial of the Single Application Fertility Regulating Device," Instruments supplied by Population Research, Inc., Clearwater, Florida.

Presented at the Ninetieth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Virginia, September 5-8, 1979.

Reprint requests: Dr. Robert S. Neuwirth, Department of Obstetrics and Gynecology, St. Luke's Hospital, 1111 Amsterdam Ave., New York, New York 10025.

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REFERENCES

1. Richart, R. M., Neuwirth, R. S., and Bolduc, L.: Single application fertility regulating device: Description of a new instrument, *AM. J. OBSTET. GYNECOL.* 127:86, 1977.
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P020014

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Conceptus_o

June 22, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
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Rockville, MD 20850

RE: Amendment to PMA No. P020014
Response to Agency Request for Articles on Ovabloc and Femcept Device
Conceptus EssureTM System for Permanent Birth Control

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JUN 24 10 07 AM '02
FDA/CDRH/OCE/DMC

Dear (b) (6)

The Agency requested that we supply a copy of published articles regarding the Ovabloc (silicone plug) and Femcept (methylcyanoacrylate) tubal occlusion devices. A literature search was conducted and the publication lists are provided in Attachment A and B, respectively. A copy of each of the articles referenced follows each respective list, with the exception of two articles on Ovabloc, which we have ordered from foreign journals but have not yet been received (#4, van der Leij and #7, Loffer). We will supply these articles once received.

In addition, although not requested, we can supply copies of articles for the following tubal occlusion devices, which have been tested clinically by other researchers: P-block (Hydrogel-nylon), Hamou Plug (Nylon), and the Hosseinian UTJ device (Polymer-Elgiloy). Please let us know if the Agency would like this additional information to be submitted.

If you have any questions, I can be reached at (b) (6), or by fax at (b) (6) or by e-mail at (b) (6)

Sincerely
(b) (6)

Enclosures: Attachment A and B (2 copies)

Table of Contents

Attachment A

1. Final Product Device Testing Table
2. E0749
3. R1553

E0749

E1907

R1553

Table of Contents

Attachment C

1. Test Criteria Table
2. R0732
3. R0667

R0732

R0667

APPENDIX I

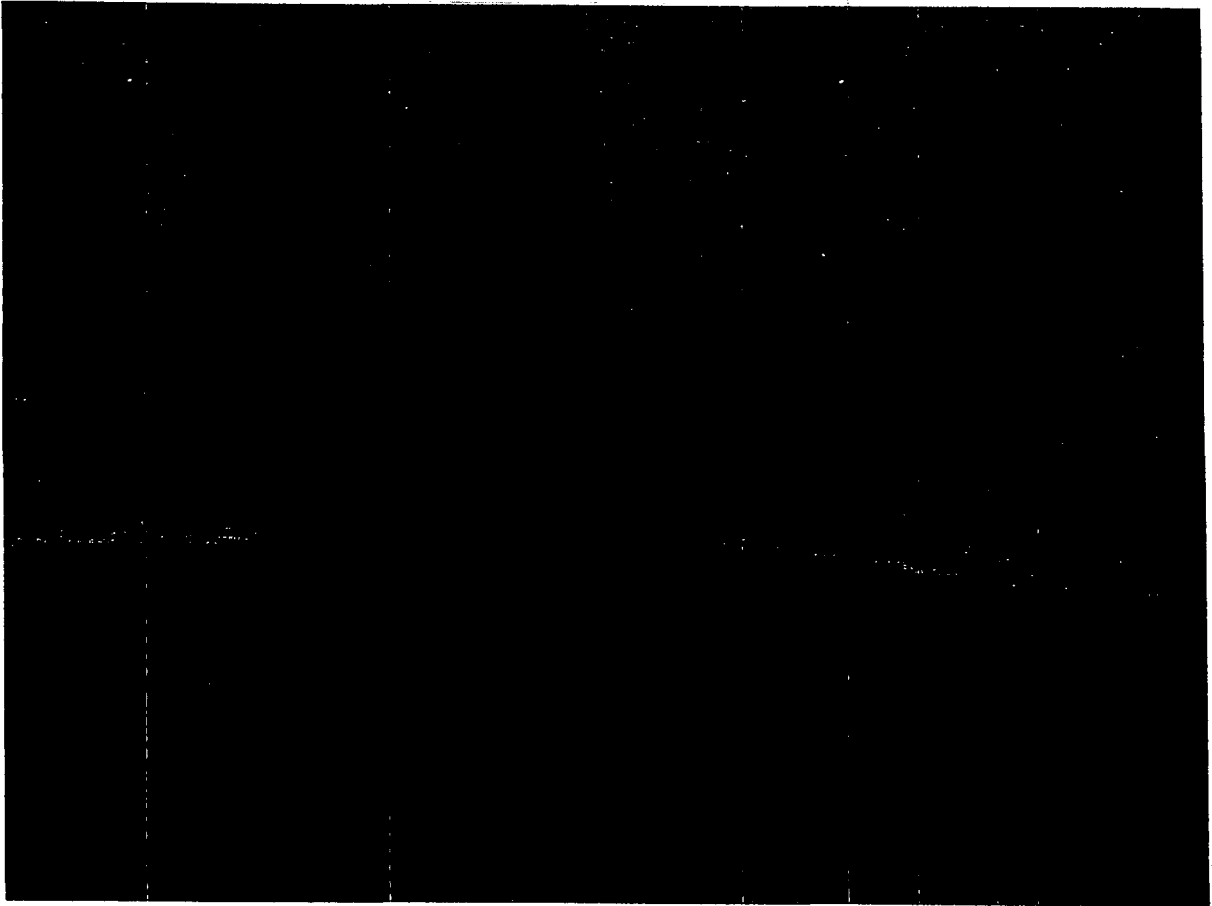
VIBRATION CONTROL SPECTRA

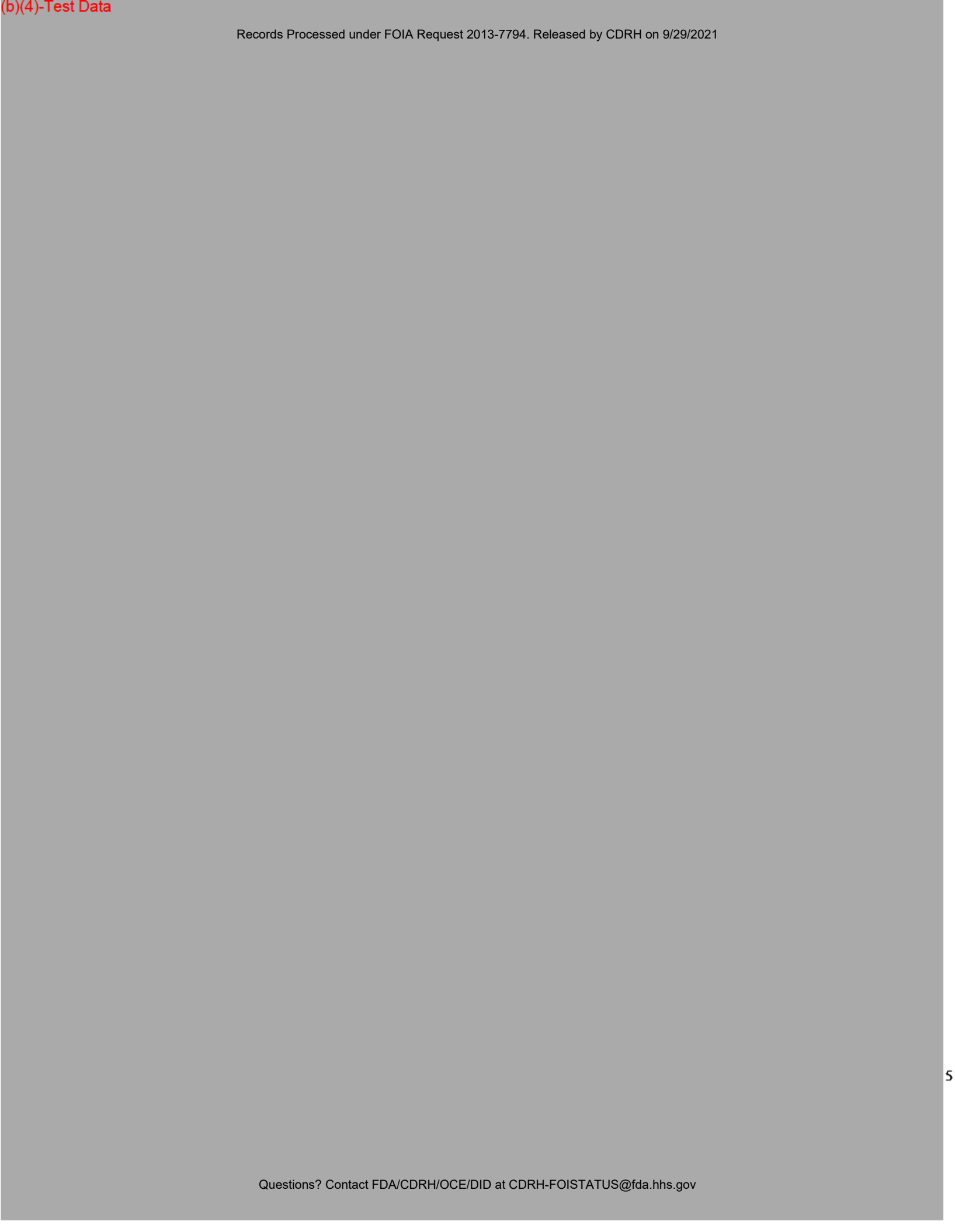
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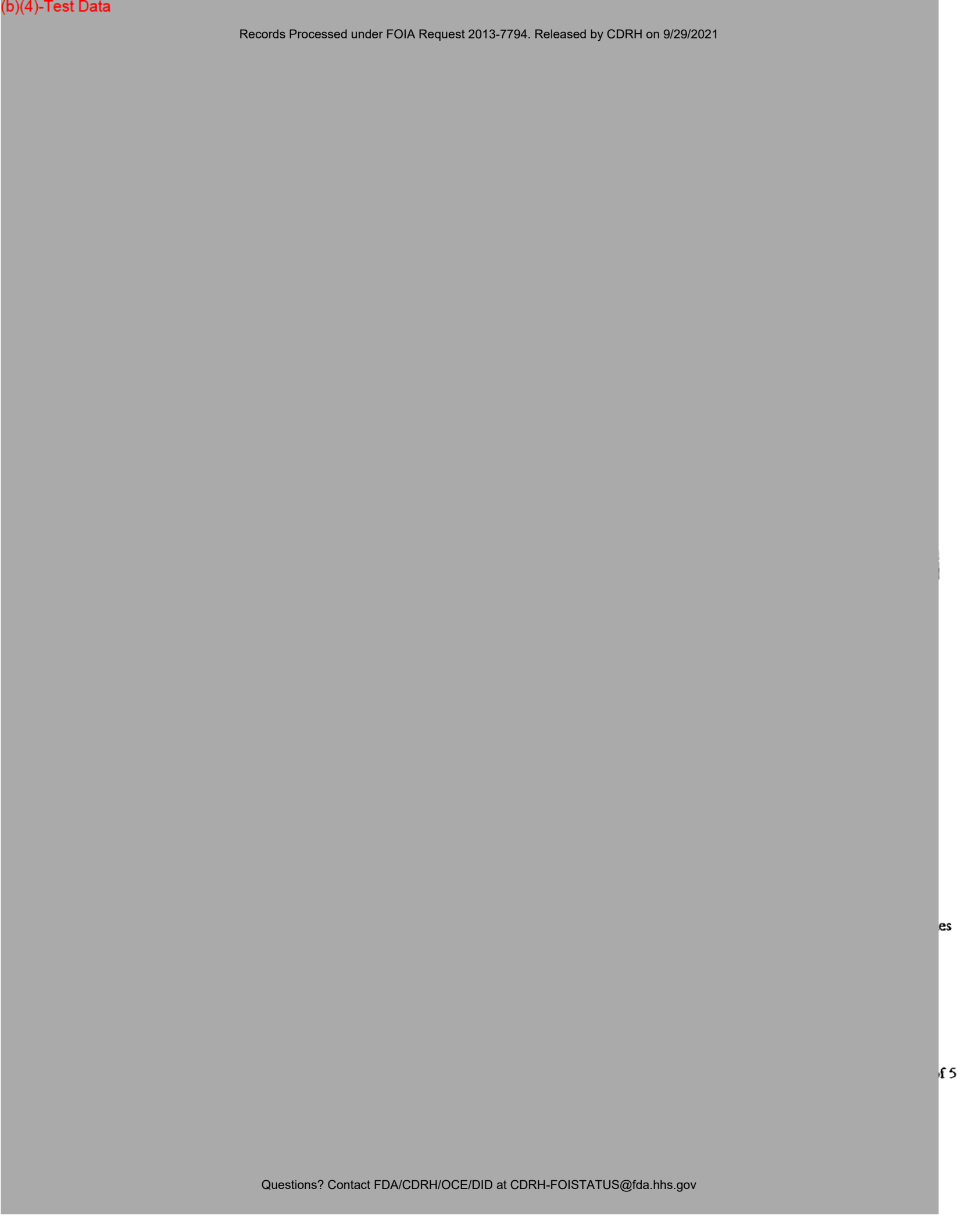
APPENDIX II

SEAL STRENGTH DATA

(b)(4)







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APPENDIX I

CONDITIONING CHART

(b)(4)

APPENDIX II
COMPRESSION TEST DATA

(b)(4)

APPENDIX III

VIBRATION TEST DATA

(b)(4)

PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A007 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.

SHORT NAME CONCEPTUS

CONTACT (b) (6)

DIVISION _____

ADDRESS 1021 HOWARD AVE.

SAN CARLOS, CA 94070

PHONE NO. (b) (6)

FAX NO. (650) 610-8363

MANUFACTURER CONCEPTUS, INC.

REG NO. 2951250

(b) (4)

(b) (4)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 21-JUN-2002

DATE RECEIVED IN ODE 24-JUN-2002

CYCLE # 1

CYCLE START 22-APR-2002

DATE FILING DUE _____

DATE DECISION DUE _____

	ELAPSED	LAST CYCLE
FDA TIME	63	63
MFR TIME	0	0

AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
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C001	FILE	22-APR-2002	
A001	UMIN	03-MAY-2002	
A002	UMIN	16-MAY-2002	
A003	UMIN	28-MAY-2002	
A004	UMIN	07-JUN-2002	
A005	UMIN	13-JUN-2002	
A006	UMIN	24-JUN-2002	

P020014/A7

**DRAERD REVIEWER RECORD FOR ORIGINAL 510(K)s,
AND PMA AND IDE SUPPLEMENTS**

Document No. _____ Reviewer _____ Date Assigned _____

CONSULTING REVIEWS DESIGNATED, AS APPROPRIATE, BY BRANCH CHIEF AND LEAD REVIEWER, AT THE BEGINNING OF THE REVIEW:

<u>SPECIALTY</u>	<u>REVIEW NEEDED?</u>		<u>REVIEWER</u>	<u>DATES</u>	
	YES	NO		SENT	RETURNED
CLINICAL	_____	_____	_____	_____	_____
ENGINEERING/ PHYSICS	_____	_____	_____	_____	_____
CHEMISTRY/ BIOMATERIALS	_____	_____	_____	_____	_____
SOFTWARE	_____	_____	_____	_____	_____
IMMUNOLOGICAL/ STERILITY	_____	_____	_____	_____	_____
TOXICOLOGY/ BIOCOMPATIBILITY	_____	_____	_____	_____	_____
STATISTICS	_____	_____	_____	_____	_____
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A. ASSOC. DIRECTOR QC OVERVIEW: MEDICAL QC OF SUBMISSION IS NECESSARY?

YES _____ NO _____ INITIALS/DATE _____

B. IF YES IS NOTED ABOVE, MEDICAL OFFICER QC OVERVIEW:

1. Examination of the specialty reviews indicate there are remaining clinical issues that should be addressed (See attached sheet for summary).

INITIALS/DATE _____

2. In my opinion, all pertinent clinical issues have been adequately addressed.

FINAL SIGNOFF: MEDICAL OFFICER/DATE _____

FINAL SIGNOFF: ASSOC. DIRECTOR/DATE _____

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

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Office of Device Evaluation
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Rockville, Maryland 20850

June 24, 2002

(b) (6)

CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b) (6):

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A007
Dated: 21-JUN-2002
Received: 24-JUN-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (b) (6). All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

(b) (6)

Center for Devices and
Radiological Health

FROM: OMB/05E/DHC

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June 21, 2002

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Rockville, MD 20850

RE: Amendment to PMA P020014
Conceptus Essure[™] System for Permanent Birth Control
Response to FDA Questions of June 12, 2002

Dear (b) (6)

This is in response to the questions raised by the Agency in its e-mail correspondence of June 12, 2002, regarding PMA P020014 for the Essure System. Each question is repeated below in italics, followed by our response in plain text. The tables pertaining to each response are presented as Attachments and the supporting drawings, protocols, reports and instructions are presented as Appendices.

(b) (4)

(b)(4)



² Medical and Biological Effects of Environmental Pollutants, published by the National Academy of Sciences, Washington, D.C., 1975.

³ Hamilton and Minski, 1972/1973; Kehoe et al., 1940

⁴ DECOS and NEG Basis for an Occupational Standard: Platinum, 1997:14; Arbetslivsinstitutet National Institute for Working Life





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RE: Amendment to PMA P020014
Conceptus Essure[™] System for Permanent Birth Control
Response to FDA Questions of June 12, 2002

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(b) (4), (b) (6)



(b)(4)



² Medical and Biological Effects of Environmental Pollutants, published by the National Academy of Sciences, Washington, D.C., 1975.

³ Hamilton and Minski, 1972/1973; Kehoe et al., 1940

⁴ DECOS and NEG Basis for an Occupational Standard: Platinum, 1997:14; Arbetslivsinstitutet National Institute for Working Life



Table of Contents

Attachment A

1. Final Product Device Testing Table
2. E0749
3. R1553

June 21, 2002

E0749

E1907

R1553





Table of Contents

Attachment C

1. Test Criteria Table
2. R0732
3. R0667

June 21, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

R0732

R0667





APPENDIX I

VIBRATION CONTROL SPECTRA

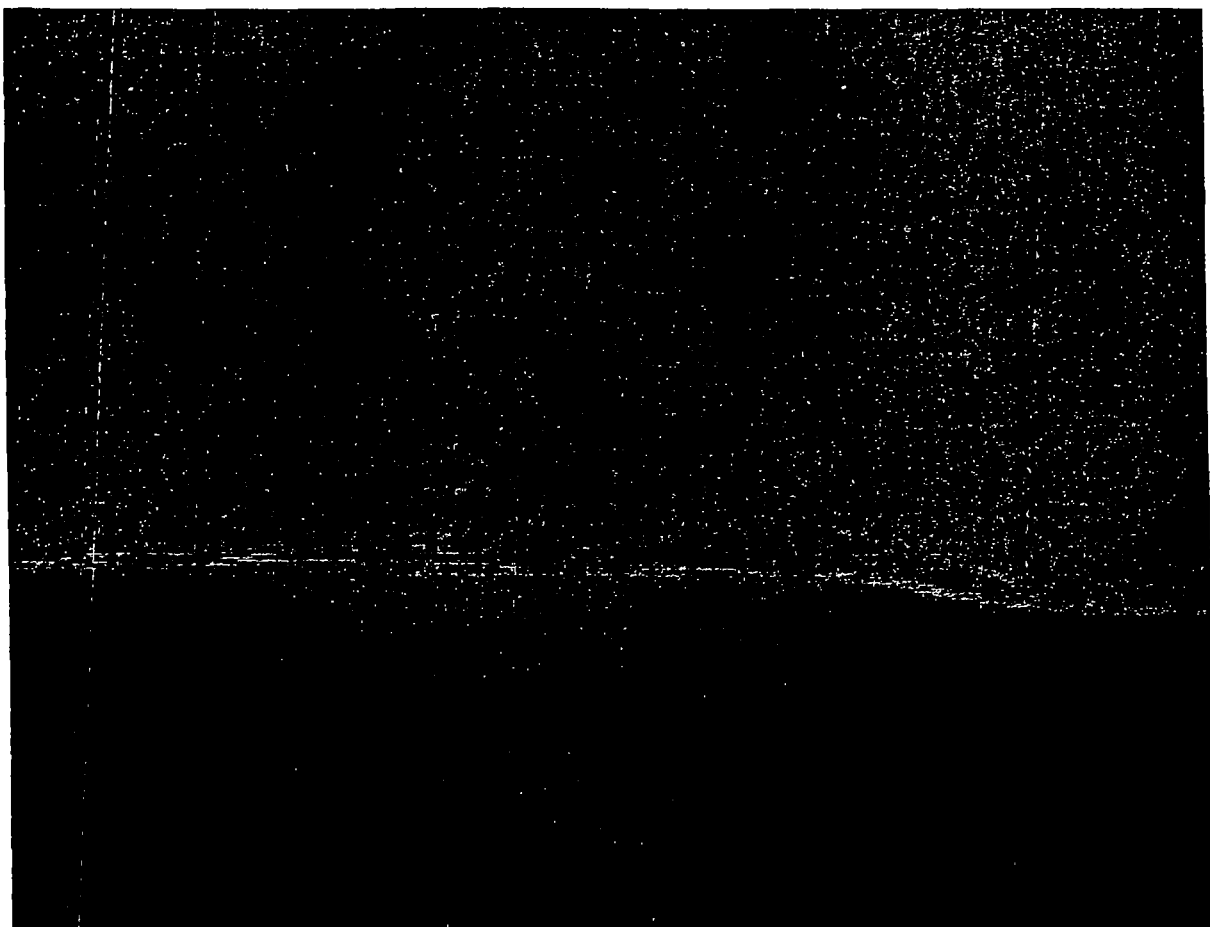
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APPENDIX II

SEAL STRENGTH DATA

(b)(4)

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APPENDIX I

CONDITIONING CHART

(b)(4)

APPENDIX II
COMPRESSION TEST DATA

(b)(4)

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APPENDIX III

VIBRATION TEST DATA

(b)(4)







Conceptus. P020014/A8/C1

July 17, 2002

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RE: Amendment to PMA No. P020014
Phase II/Pivotal Trial Update
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6):

Attached is a copy of the e-mail sent to the Agency on July 15, 2002 to update the follow-up/pregnancy status for the women in the Phase II and Pivotal Trials. In addition, an update was provided regarding the woman who became pregnant with the discontinued Beta design.

(b) (4), (b) (6)

Sincerely,

(b) (6)

505

1

Printed by: (b) (6) s
Title: **Pivotal trial/Phase II updates**

Wednesday, July 17, 2002 12:23:32 PM
Page 1 of 2



Monday, July 15, 2002 7:17:34 PM

Message

From: (b) (6) ;

Subject: Pivotal trial/Phase II updates

To:

Cc:

(b) (6)

Attachments: follow-up tables 7.13.02.doc 42K
 (b) (6) matrix.doc 40K

Per our prior discussions, and as outlined in the cover letter to our June 5, 2002 PMA Amendment (P020014), below is a summary of the updated pregnancy/follow-up status of the women in both the Phase II and Pivotal trial.

(b) (4)

(b) (4)

2

Printed by: (b) (6) ;
Title: **Pivotal trial/Phase II updates**

Wednesday, July 17, 2002 12:23:32 PM
Page 2 of 2

(b) (6), (b) (4)

Please let me know if this e-mail communication should be submitted as a formal IDE supplement to Document Control, or if notification of this information by e-mail is sufficient. Thank you.

(b) (6) ;
;
;

Conceptus, Inc.

(b) (6) ;
(650) 802-2890 fax

Table A. One-year Follow-up Status: Pivotal Trial Women with Bilateral Placement

STATUS	NUMBER
(b) (4)	

Table B. Due Dates for Pivotal Trial Women Not Yet Completing One-year Visit, N= 16

Patient No.	One-year Visit <i>Due Date</i>	Monthly Totals
(b)(4),(b)(6)		

5

Table C. Pivotal Trial Women Currently Lost-to-Follow-up, N=13

Patient No.	Last Follow-up Visit Completed	Total From Each Visit
(b) (6), (b) (4)		

le

(b)(6)-Patient Information



July 15, 2002
P020014

(b)(6)-Patient Information



8
July 15, 2002
P020014

(b)(6)-Patient Information



9

July 15, 2002
P020014

(b)(6)-Patient Information



01
July 15, 2002
P020014

Conceptus.

August 19, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
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Re: Amendment to PMA No. P020014
Correction to Adverse Event Data in Response to BIMO Audit
Conceptus Essure™ System for Permanent Birth Control

RECEIVED
AUG 21 11 07 AM '02
FDA/CDRH/OCE/DIC

Dear (b) (6) :

Conceptus is filing this PMA amendment to provide the Agency with additional data regarding adverse events noted at unscheduled study visits conducted as part of the Pivotal Trial. These adverse event data were not reflected in the most recent data submitted (in the amendment of June 5, 2002) for the above-referenced PMA.

This data discrepancy was noted during the recent (b) (6), (b) (4)
[Redacted]

Observation

"Regarding Conceptus Research Protocol STOP 2000---

Adverse events identified at unscheduled subject visits were not captured in the data submitted in the PMA. Following is a partial list of those subjects for whom unscheduled visit adverse events are not reported in data submitted with the PMA: (b) (6)
[Redacted]

The audit observation was due to the fact that our data management firm (b) (4) made a programming error in SAS that resulted in incomplete reporting of some adverse events. Specifically, adverse events that were contained within the raw data and recorded on the electronic Case Report Forms at unscheduled visits were not included in the Adverse Event Report supplied by (b) (4) to Conceptus. As a result, these same adverse events were not included in the data submitted for the Essure PMA.

Corrective Actions Taken by Conceptus

Conceptus contacted (b) (4) immediately regarding this error and asked them to investigate this incident. [Redacted] indicated that to prevent such an occurrence, a cross-validation of the

adverse event data was performed prior to the generation of the reports they provided to Conceptus. In this cross-validation step, they compared the number of positive answers to the question "Did the participant experience any adverse events" to the number of adverse events in their report. This cross-validation did not reveal the programming error, however, since the Unscheduled Visit Case Report Form does not include this question "Did the participant experience any adverse events" but instead, includes an instruction to complete an Adverse Event form if one was reported at the Unscheduled visit.

Conceptus, (b) (4) has taken the following actions to correct this finding:

1. (b) (4)
2. (b) (4)
3. (b) (4)
4. (b) (4)
5. (b) (4)
6. A Corrective and Preventive Action ((b) (4)) was initiated by Conceptus to address this observation.


Clinical Data Corrections Resulting From Audit Observation

On July 19, 2002, Conceptus filed a formal response to the audit observation referenced above. As indicated in the response, we are amending the PMA herein to include revisions to the following documents originally submitted in the June 5, 2002 PMA amendment:

- 1) Revised Tables 42, 44 and 46 (Volume 2, pages 88, 92 and 96 of June 5, 2002 PMA Amendment);
- 2) Updated "Adverse Events after the day of the procedure up to one year visit" data listing (Volume 10, Section 19 of June 5, 2002 PMA Amendment)
- 3) Updated "Adverse Events" listing by site (Volume 2, Exhibit K of June 5, 2002 PMA Amendment).

The three above-listed items are presented in **Exhibit A**, **Exhibit D** and **Exhibit E**, respectively. Please note that two of the patients noted in FDA's audit finding (b) (6) (b) (6) are not included in the revised data table presented in **Exhibit D**, for the following reasons:

(b) (4), (b) (6)



(b) (4)

While we regret this error in data management, we believe that the safety data in the PMA are not significantly changed from what was originally submitted in the June 5, 2002 PMA Amendment.

If there are questions regarding this application, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)



Table 42. Changes in menstrual function reported at follow-up visits

Follow-up visit	Irregular menses	Bleeding between Menses	Heavier than usual menstrual flow	Less than usual menstrual flow
(b)(4)				

Table 44. Pelvic pain

	Pelvic pain				
Follow-up visit	Dysmenorrhea	Dyspareunia	Ovulatory pain	Other Pelvic***	

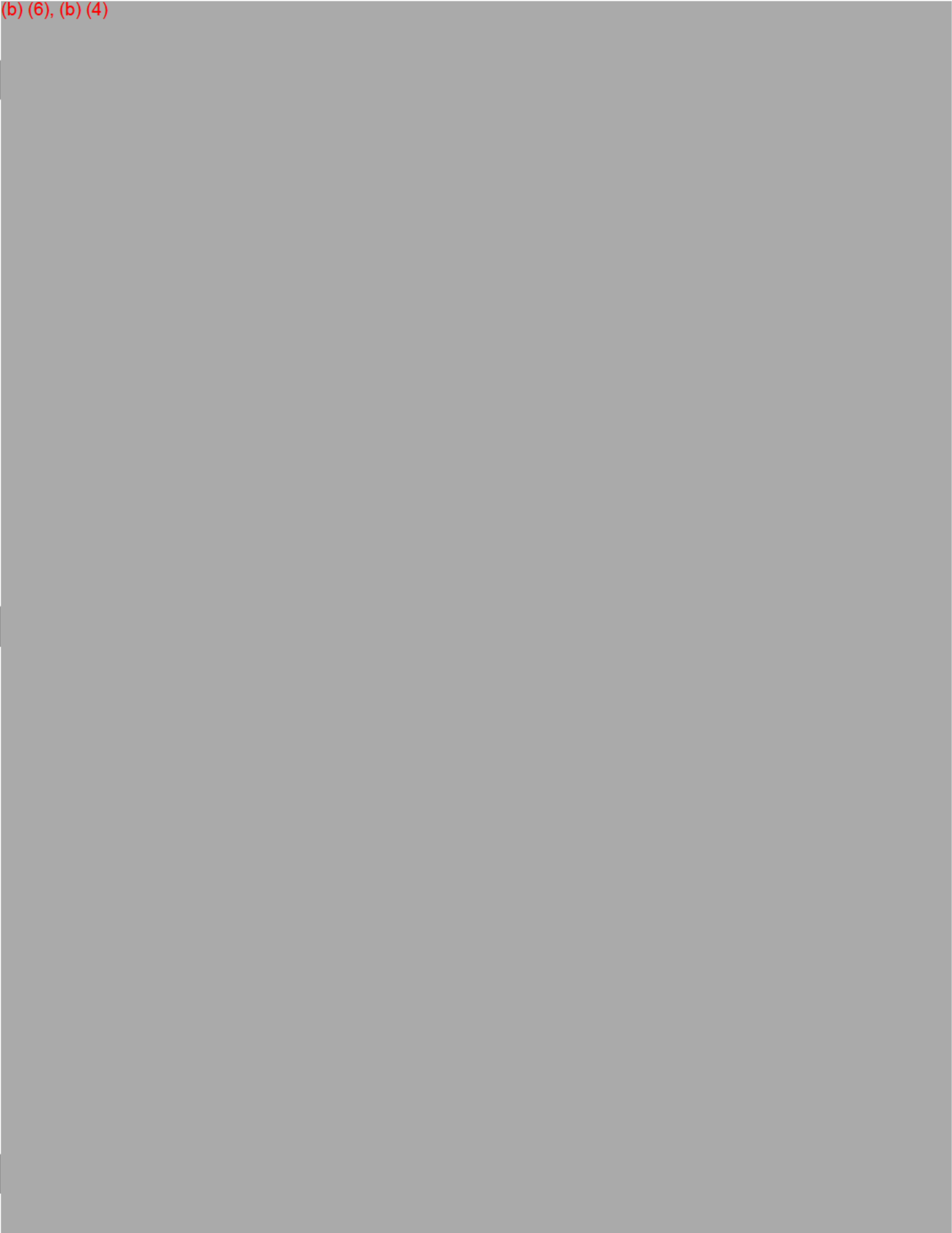
(b)(4)



Table 46. Adverse Events by Body System rated by Investigator as at least possibly related: For the First Year of Reliance*
N = 476 (patients with at least 1 Micro-insert)

Adverse Event	Number	Percent
(b)(4)		

(b) (6), (b) (4)



August 14, 2002
Page 2 of 2

(b) (6), (b) (4)




Table 144. Essure Systems Used per Tube per Procedure for All Cases

N	Mean	Stddev	Median	Min	Max
(b)(4),(b)(6)					

(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021

(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021

(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021

(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



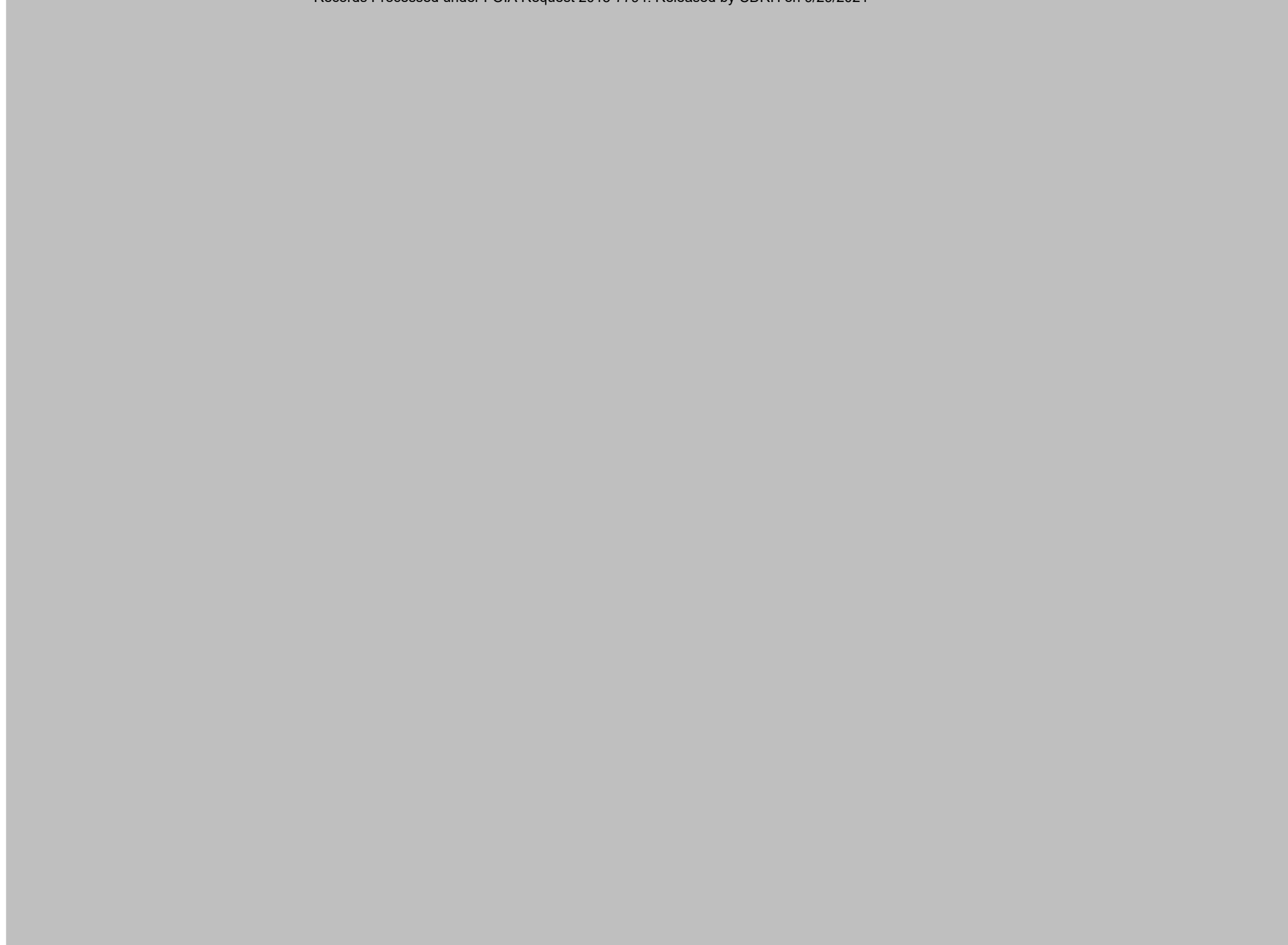
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Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



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Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



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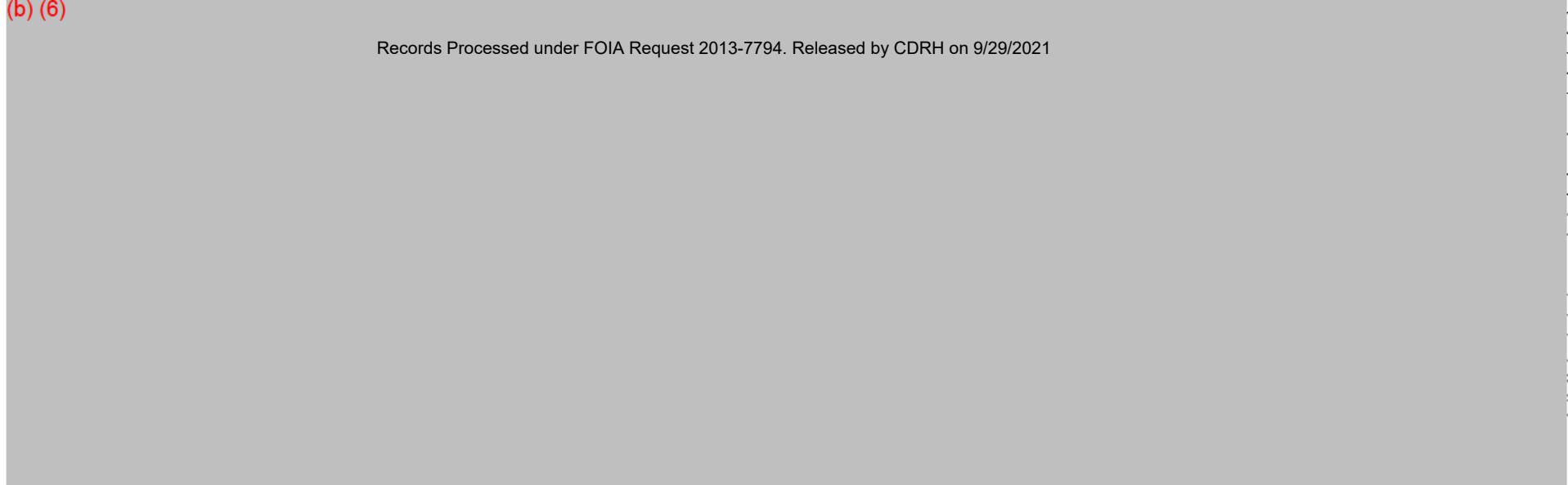
(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



(b) (6)

Records Processed under FOIA Request 2013-7794. Released by CDRH on 9/29/2021



Adverse events by site (Table number refers to Pivotal trial report table number)

Site	Investigator	Subject Number	Table Number	Adverse Event
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(b) (6)



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CDRH SUBMISSION COVER SHEET

Date of Submission: August 20, 2002

FDA Document Number: PMA P020014

Section A Type of Submission

PMA	PMA Supplement	PDP	510(k)	Meeting
<input type="checkbox"/> Original submission <input type="checkbox"/> Modules submission <input checked="" type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment	<input type="checkbox"/> Regular <input type="checkbox"/> Special <input type="checkbox"/> Panel Track <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA Supplement	<input type="checkbox"/> Presubmission summary <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of intent to start clinical trials <input type="checkbox"/> Intention to submit Notice of Completion <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated <input type="checkbox"/> Additional information <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated	<input type="checkbox"/> Pre-IDE meeting <input type="checkbox"/> Pre-PMA meeting <input type="checkbox"/> Pre-PDP meeting <input type="checkbox"/> 180-day meeting <input type="checkbox"/> Other (specify):
IDE	Humanitarian Device Exemption	Class II Exemption	Evaluation of Automatic Class III Designation	Other Submission
<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	Describe submission:

Section B Applicant or Sponsor

Company / Institution name: Conceptus Incorporated		Establishment registration number: 2951250	
Division name (if applicable): Not Applicable		Phone number (include area code): (b) (6)	
Street address: 1021 Howard Avenue		FAX number (include area code): (650) 802-2890	
City: San Carlos	State/Province: CA 94070	Country: USA	
Contact name: (b) (6)			
Contact title: (b) (6)		Contact e-mail address: (b) (6)	

Section C Submission correspondent (if different from above)

Company/Institution name: Same as above		Establishment registration number: Same as above	
Division name (if applicable): Same as above		Phone number (include area code): (b) (6)	
Street address: Same as above		FAX number (include area code): Same as above	
City: Same as above	State/Province: Same as above	Country: Same as above	
Contact name: Same as above			
Contact title: Same as above		Contact e-mail address: Same as above	

Section D1	Reason for Submission - PMA, PDP, or HDE	
<input checked="" type="checkbox"/> New device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or expanded indications <input type="checkbox"/> Licensing agreement <input type="checkbox"/> Process Change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Sterilization <input type="checkbox"/> Packaging <input type="checkbox"/> Other (specify below) <input type="checkbox"/> Response to FDA correspondence: <input type="checkbox"/> Request for applicant hold <input type="checkbox"/> Request for removal of applicant hold <input type="checkbox"/> Request for extension <input type="checkbox"/> Request to remove or add manufacturing site <input type="checkbox"/> Other reason (specify):	<input type="checkbox"/> Change in design, component, or specifications: <input type="checkbox"/> Software <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (specify below) <input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager <input type="checkbox"/> Distributor <input type="checkbox"/> Report submissions: <input type="checkbox"/> Annual or periodic <input type="checkbox"/> Post-approval study <input type="checkbox"/> Adverse reaction <input type="checkbox"/> Device defect <input type="checkbox"/> Amendment <input type="checkbox"/> Change in ownership <input type="checkbox"/> Change in correspondent
Section D2	Reason for Submission - IDE	
<input type="checkbox"/> New device <input type="checkbox"/> Addition of institution <input type="checkbox"/> Expansion/extension of study <input type="checkbox"/> IRB certification <input type="checkbox"/> Request hearing <input type="checkbox"/> Request waiver <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of application <input type="checkbox"/> Unanticipated adverse effect <input type="checkbox"/> Notification of emergency use <input type="checkbox"/> Compassionate use request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continuing availability request <input type="checkbox"/> Other reason (specify):	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent <input type="checkbox"/> Design <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing process <input type="checkbox"/> Protocol - feasibility <input type="checkbox"/> Protocol - other <input type="checkbox"/> Sponsor <input type="checkbox"/> Report Submission: <input type="checkbox"/> Current investigator <input type="checkbox"/> Annual progress <input type="checkbox"/> Site waiver limit reached <input type="checkbox"/> Final	<input type="checkbox"/> Response to FDA letter concerning: <input type="checkbox"/> Conditional approval <input type="checkbox"/> Deemed approved <input type="checkbox"/> Deficient final report <input type="checkbox"/> Deficient progress report <input type="checkbox"/> Deficient investigator report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request extension of time to respond to FDA <input type="checkbox"/> Request meeting
Section D3	Reason for Submission - 510(k)	
<input type="checkbox"/> New device <input type="checkbox"/> Addition or expanded indications <input type="checkbox"/> other reason (specify):	<input type="checkbox"/> Change in technology <input type="checkbox"/> Change in design	<input type="checkbox"/> Change in materials <input type="checkbox"/> Change in manufacturing process

Section E Additional Information on 510(k) Submissions					
Product codes of devices to which substantial equivalence is claimed:				Summary of, or statement concerning, safety and effectiveness data:	
1	2	3	4	<input type="checkbox"/> 510 (k) summary attached <input type="checkbox"/> 510 (k) statement	
5	6	7	8		
Information on devices to which substantial equivalence is claimed:					
510(k) Number	Trade or proprietary or model name			Manufacturer	
1	1			1	
2	2			2	
3	3			3	
4	4			4	
5	5			5	
6	6			6	
Section F Product Information - Applicable to All Applications					
Common or usual or classification name: Device, Occlusion, Tubal, Contraceptive					
Trade or proprietary or model name			Model number		
1 Essure (formerly STOP Device) System			PCD 001/ ESS001		
2					
3					
4					
5					
FDA document numbers of all prior related submissions (regardless of outcome):					
1 G960052	2 G960206	3 G980152	4 G000055	5 G010223	6 I010191
7 M010031/I	8 M010031/II	9 M010031/III	10 M010031/IV	11 M010031/V	12 PMA P020014
Data included in submission : <input checked="" type="checkbox"/> Laboratory testing <input type="checkbox"/> Animal trials <input type="checkbox"/> Human trials					
Section G Product Classification - Applicable to All Applications					
Product code: KNH	C.F.R. section 884.5380		Device class: <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input checked="" type="checkbox"/> Class III <input type="checkbox"/> Unclassified		
Classification panel: Obstetrics/Gynecology					
Indications (From labeling): The Essure™ System is indicated for permanent birth control (female sterilization) by occlusion of the fallopian tubes.					

<p>Note: Submission of this information does not create the need to submit a 2891 or 2891a Device Establishment Registration form.</p>		<p>FDA Document Number:</p>	
<p>Section H Manufacturing/ Packaging / Sterilization Sites</p>			
<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number: 2951250	<input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/relabeler
Company/institution name: Conceptus Incorporated		Establishment registration number: 2951250	
Division name (if applicable): Not Applicable		Phone number (include area code): (b) (6)	
Street address: 1021 Howard Avenue		Fax number (include area code): (650) 802-2890	
City: San Carlos	State/Province: CA	Country: USA	ZIP/Postal Code: 94070
Contact Name: (b) (6)			
Contact Title: (b) (6) Affairs		Contact e-mail address: (b) (6)	
<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number: 2011171	<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input checked="" type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/ relabeler
Company/institution name: (b) (4)		Establishment registration number:	
Division name (if applicable): N/A		Phone number (include area code): (b) (4), (b) (6)	
(b) (4)		Fax number (include area code): (b) (4)	
City: (b) (4)	State/Province: (b) (4)	Country: USA	ZIP/Postal Code: (b) (4)
Contact Name: (b) (4), (b) (6)			
Contact Title: (b) (4), (b) (6)		Contact e-mail address:	
<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete	FDA establishment registration number:	<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract manufacturer	<input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Repackager/ relabeler
Company/institution name:		Establishment registration number:	
Division name (if applicable):		Phone number (include area code): ()	
Street address:		Fax number (include area code): ()	
City:	State/Province:	Country:	ZIP/Postal Code:
Contact Name:			
+Contact Title:		Contact e-mail address:	

Conceptus, Inc.

Conceptus®

August 20, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED
AUG 21 11 05 AM '02
FDA/CDRH/OCE/DMC

Re: Amendment to PMA No. P020014
Response to FDA Questions (Fax of 8/5/2002 and e-mail of 8/6/2002)
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

This is in response to the questions raised by the Agency on August 5, 2002 (fax) and August 6, 2002 (e-mail) regarding PMA P020014. This PMA Amendment contains our response to the Engineering, Corrosion and Shelf Life questions only. Clinical, Post-Approval Study, MRI and labeling questions will be addressed under a separate cover. Please note that our responses to Questions #1 and #2 below were faxed to the Agency on August 9, 2002, and those same responses are being resubmitted in this Amendment. Your questions are presented below in italics, followed by our response in plain text.

This amendment also includes information on a pregnancy in a commercial patient that received only unilateral Essure placement. This pregnancy was reported to the Agency by (b) (6) (b) (6) via e-mail, on August 8, 2002. A copy of (b) (6) e-mail to FDA is included in **Appendix A** of this submission.

(b) (4)

[Redacted content]

(b) (4)



(b) (4)



(b) (4)



¹ Hoffland Environment. http://www.hofflandenv.com/Systems/Hydroxide_Precip.htm updated on 02-11-00

(b) (4)



(b) (4)



(b) (4)



Conceptus, Inc.

(b) (4)



Table 4 – Effects of Solder Bond on Mechanical Integrity and Radiopacity

Solder Bond	Purpose	Effect on mechanical integrity and radiopacity
(b) (4)		

Figure 3 – Inner Coil to Outer Coil Solder Bond

(b) (4)



(b) (4)



(b) (4)




(b) (4)



Conceptus, Inc.

(b) (6), (b) (4)

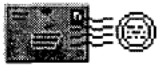


Printed by: (b) (6)

Friday, August 16, 2002 8:59:04 AM

Title: **Pregnancy in Commerical Patient with Unilateral Essure Placement**

Page 1 of 2



Thursday, August 08, 2002 4:48:37 PM

Message

From: (b) (6)

Subject: Pregnancy in Commerical Patient with Unilateral Essure Placement

To: (b) (6)

Cc: (b) (6)

(b) (4)


Printed by: (b) (6)

Friday, August 16, 2002 8:59:04 AM

Title: **Pregnancy in Commerical Patient with Unilateral Essure Placement**

Page 2 of 2

(b) (6), (b) (4)



APPENDIX I

CONDITIONING CHART

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APPENDIX II

COMPRESSION TEST DATA

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APPENDIX III

VIBRATION TEST DATA

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LDC

PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A011 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.

SHORT NAME CONCEPTUS

CONTACT (b) (6)

DIVISION _____

ADDRESS 1021 HOWARD AVE.

SAN CARLOS, CA 94070

PHONE NO. (b) (6)

FAX NO. (650) 610-8363

MANUFACTURER CONCEPTUS, INC.

REG NO. 2951250

(b) (4)

(b) (4)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 08-JUL-2002

DATE RECEIVED IN ODE 23-AUG-2002

DATE FILING DUE _____

DATE DECISION DUE _____

CYCLE # 1
CYCLE START 22-APR-2002

	ELAPSED	LAST CYCLE
FDA TIME	123	123
MFR TIME	0	0

AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
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C001	<u>FILE</u>	<u>22-APR-2002</u>	
A001	<u>UMIN</u>	<u>03-MAY-2002</u>	
A002	<u>UMIN</u>	<u>16-MAY-2002</u>	
A003	<u>UMIN</u>	<u>28-MAY-2002</u>	
A004	<u>UMIN</u>	<u>07-JUN-2002</u>	
A005	<u>UMIN</u>	<u>13-JUN-2002</u>	
A006	<u>UMIN</u>	<u>24-JUN-2002</u>	
A007	<u>UMIN</u>	<u>24-JUN-2002</u>	
A008	<u>UMIN</u>	<u>18-JUL-2002</u>	
A009	<u>UMIN</u>	<u>21-AUG-2002</u>	
A010	<u>UMIN</u>	<u>21-AUG-2002</u>	

P020014/AT1

DRAERD REVIEWER RECORD FOR ORIGINAL 510(K)s,
AND PMA AND IDE SUPPLEMENTS

Document No. _____ Reviewer _____ Date Assigned _____

*CONSULTING REVIEWS DESIGNATED, AS APPROPRIATE, BY BRANCH CHIEF AND LEAD REVIEWER,
AT THE BEGINNING OF THE REVIEW:*

<u>SPECIALTY</u>	<u>REVIEW NEEDED?</u>		<u>REVIEWER</u>	<u>DATES</u>	
	YES	NO		SENT	RETURNED
CLINICAL	_____	_____	_____	_____	_____
ENGINEERING/ PHYSICS	_____	_____	_____	_____	_____
CHEMISTRY/ BIOMATERIALS	_____	_____	_____	_____	_____
SOFTWARE	_____	_____	_____	_____	_____
IMMUNOLOGICAL/ STERILITY	_____	_____	_____	_____	_____
TOXICOLOGY/ BIOCOMPATIBILITY	_____	_____	_____	_____	_____
STATISTICS	_____	_____	_____	_____	_____
OTHER _____	_____	_____	_____	_____	_____

COMMENTS:-

REVISED 1/2/96 LMS
ON LAN AS REVREC.FUM

QUALITY CONTROL OVERVIEW OF DOCUMENT

A. ASSOC. DIRECTOR QC OVERVIEW: MEDICAL QC OF SUBMISSION IS NECESSARY?

YES _____ NO _____ INITIALS/DATE _____

B. IF YES IS NOTED ABOVE, MEDICAL OFFICER QC OVERVIEW:

1. Examination of the specialty reviews indicate there are remaining clinical issues that should be addressed (See attached sheet for summary).

INITIALS/DATE _____

2. In my opinion, all pertinent clinical issues have been adequately addressed.

FINAL SIGNOFF: MEDICAL OFFICER/DATE _____

FINAL SIGNOFF: ASSOC. DIRECTOR/DATE _____

REVISED: 1/2/96 LMS
LOCATED ON LAN AS REVREC.FRM

P020014/A11
Public Health Service

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

August 23, 2002

(b) (6)
CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A011
Dated: 08-JUL-2002
Received: 23-AUG-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (b) (6). All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

(b) (4)

Center for Devices and
Radiological Health

Conceptus.

July 8, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Amendment to PMA No. P020014
Additional Articles on Ovabloc
Conceptus Essure™ System for Permanent Birth Control

RECEIVED
AUG 23 10 53 AM '02
FDA/CDRH/OCE/DMC

Dear (b) (6) :

This is to follow-up our June 22, 2002 PMA amendment. That amendment was submitted to respond to the Agency's request for a copy of published articles regarding the Ovabloc (silicone plug) and Femcept (methylcyanoacrylate) tubal occlusion devices. A literature search was conducted and the publication lists and corresponding articles were provided in Attachment A and B, respectively, of the June 22, 2002 PMA amendment. As stated in the PMA amendment, however, two articles on Ovabloc were ordered from foreign journals and as such, were not received at the time of the amendment. We have since received these articles, and they are attached here. These articles correspond to #4 (van der Leij) and #7 (Loffer) of the publication list submitted in Attachment A of the June 22, 2002 amendment.

Also, as stated in the June 22, 2002 amendment, we can supply copies of articles for the following other tubal occlusion devices, which have been tested clinically by other researchers: P-block (Hydrogel-nylon), Hamou Plug (Nylon), and the Hosseinian UTJ device (Polymer-Elgiloy). We will await instruction from the Agency regarding whether this additional information should be submitted.

If you have any questions regarding this amendment, I can be reached at (b) (6), or by fax at (b) (6), or by e-mail at (b) (6). Thank you.

Sincerely,

(b) (6)

Sps

LEARNING HYSTEROSCOPY STERILIZATION AND THE OVABLOC SYSTEM WITH HYSKON

F.D. Loffer, M.D., P.S. Loffer, R.N.
Phoenix, Arizona

A review of the first 100 and the last 100 patients in a series of 268 patients sterilized by hysteroscopic injection of liquid silicone into the fallopian was made to evaluate the success rate as it relates to experience with the procedure.

The two groups were similar in composition. While the percentage of patients sterilized increased only from 91% in the first 100 patients to 94% in the last 100 patients the numbers that were sterilized at the time of the first procedure increased by 9%. The two major reasons for repeated procedures were tip separation and tubal spasm. The former may become less of a problem with new manufacturing changes. Tubal spasm was reduced as a problem by controlling the temperature of Hyskon but it remains a difficult problem in a smaller number of patients even in the last group. Other causes for repeated procedures were primarily related to operator inexperience and investigational problems. They appear not to be a significant problem for physicians who will learn this procedure in future. This procedure is well received by patients. Hysteroscopists will find it a valuable outpatient female sterilization technique.

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D. Loffer et al.
Hysteroscopy sterilization

(b)(4)-Copyrighted Material



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References

- 1) Erb R.A.: Hysteroscopic sterilization with formed in-place silicone rubber plugs: Basic process and instruments, in Stegler A.M., and Lindemann H.J., (eds): *Hysteroscopy Principles and Practice*, Philadelphia, 1984, J.B. Lippincott, pp. 257-265.
- 2) Reed T.P., Erb R.A.: Hysteroscopic tubal occlusion with silicone rubber, *Obstet. Gynecol.* 61: 388, 1983.
- 3) Loffer F.D., Loffer P.S.: Learning hysteroscopic sterilization using the ovabloc system with hyskon. *Consendonk Conference*, Belgium, June 1984.
- 4) Loffer F.D.: Hysteroscopic sterilization with the formed in-place silicone plugs, *Am. J. Obstet. Gynecol.* 149: 261, 1984.

International Journal of Gynecological Pathology
14:167-173, Raven Press, Ltd., New York
© 1995 International Society of Gynecological Pathologists

Impact of Ovabloc Intratubal Polymer on the Morphology of the Fallopian Tube

G. van der Leij, M.D., and C. van Krimpen M.D., Ph.D.

Summary: Treatment of the fallopian tubes by Ovabloc silicone intratubal polymer (ITP; Dow Corning silastic 382 Medical-Grade Elastomer) is used for permanent female contraception. Studies on animals show minor structural changes in the tubal epithelial lining caused by the ITP and suggest reversibility of tubal integrity after removal of the polymer. The aim of this study was to examine the impact of the ITP on the human tubal epithelial lining. From 13 patients treated with ITP, 23 fallopian tubes were studied by light microscopy and transmission electron microscopy. The examined 19 isthmic and 10 ampullary parts show marked structural changes. In the isthmic parts of the fallopian tubes, cellular and ciliary changes develop immediately after insertion of the silicone polymer. As for the ampullary parts, the cellular and ciliary changes are related to the ITP exposure time. The changes in the isthmus and ampulla are persistent for at least 15 months after removal of the ITP. It is not known whether the effects are reversible. **Key Words:** Ovabloc—Silicone—Intratubal polymer—Contraception—Oviductal epithelium.

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From the Department of Gynaecology and Obstetrics, Schieland Hospital, Schiedam (G.L.), and the Department of Pathology, Diagnostic Centre SSDZ, Delft (C.K.), The Netherlands.

Address for correspondence and reprint requests to Dr. G. van der Leij, Department of Gynaecology and Obstetrics, Schieland Hospital, P.O. Box 215, 3115 AE Schiedam, The Netherlands.

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REFERENCES

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5. Loffer FD. Hysteroscopic sterilisation with the use of formed-in-place silicone plugs. *Am J Obstet Gynaecol* 1984; 149:261-70.
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9. Bloom W, Fawcett DW. The oviduct, or fallopian tube. In: *A textbook of histology*. Philadelphia, PA: WB Saunders, 1962:599-601.
10. Ham AW. *Histology*. VIIth ed. Philadelphia, PA: JB Lippincott, 1974:96.
11. Donnez J, Canasas-Roux F, Caprasse J. Cyclic changes in

IMPACT OF POLYMER ON MORPHOLOGY

- ciliation, cell height, and mitotic activity in human tubal epithelium during reproductive live. *Fertil Steril* 1985;43:544-60.
12. Tam PP, Mao KR, Lai FM. The ultrastructural changes of the mucosa of blocked fallopian tubes. *Br J Obstet Gynaecol* 1988;95:802-7.
 13. Fedele L, Zamberletti D, Marchini M, Verceline P, Cavalli G. Degree of endosalpingeal deciliation (by S.E.M.) in hydrosalpinx is not prognostic for post-surgical fertility. *Acta Eur Fertil* 1984;15:199-205.
 14. Luri M, Tut-Kaspa I, Weill S, Goldenberg S. Ciliary ultrastructure of respiratory and fallopian tube epithelium in a steril women with Kartagener's syndrome. A quantitative estimation. *Chest* 1989;95:578-81.
 15. Afzelius BA, Camner P, Mossberg B. On the function of cilia in the female reproductive tract. *Fertil Steril* 1978;29:72.

FDA/CDRH/OCE/DID

SEP 4 11 37 AM '02

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P020014/A12

Conceptus, Inc.

Conceptus®

September 3, 2002

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SEP 4 11 37 AM '02

FDA/CDRH/DO

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: Amendment to PMA No. P020014
Submission of 9-Month Interim Report of Real Time Aging Study
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

Conceptus Inc. is hereby submitting a 9-Month Interim Report of its Real Time Aging Study of the Essure System. The Real Time Aging study is currently ongoing to demonstrate both package integrity and functional performance of the Essure System for a period of two years. Provided in **Exhibit A** are the results after 9 months of Real Time testing. Testing was done according to the previously submitted protocol (Module IV, PMA P020014, April 15, 2002) and is included again in this submission as **Exhibit B**.

This 9-Month Interim Report follows the submission of the 6-Month Real Time Aging Study results (PMA Amendment dated June 21, 2002) and the Real Time Aging Study protocol and 3-Month Interim Report submitted to the Agency in Module IV (pages 000024-000034) of PMA No. P020014, April 15, 2002.

We believe that the data presented in this Amendment and the results of the 2-Year Accelerated Aging Study submitted on May 15, 2002, are adequate to support a two-year expiration date for the Essure System.

Please note that results of the 12-Month and 2-Year Real Time Aging study will be submitted to the Agency as soon as the data is available (projected dates: December 2002 and December 2003).

2

Conceptus, Inc.

If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)



3

APPENDIX I

CONDITIONING CHART

(b)(4)

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22

APPENDIX II

COMPRESSION TEST DATA

(b)(4)

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APPENDIX III

VIBRATION TEST DATA

(b)(4)

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26

P020014 1A13

Conceptus, Inc.

Conceptus[®]

September 13, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: Amendment to PMA No. P020014
Formal submission of previously submitted e-mail communications
Conceptus Essure[™] System for Permanent Birth Control

RECEIVED
SEP 16 11 51 AM '02
FDA/CDRH

Dear (b) (6):

Conceptus Inc. is hereby submitting this PMA Amendment to provide hard copies of the e-mail communication between Conceptus and the Agency (b) (6) just prior to the panel meeting. The e-mails included in this submission are as follows:

- Attachment A** E-mail communication from (b) (6) (b) (6) dated July 14, 2002
- Attachment B** E-mail communication from (b) (6) (b) (6) dated July 17, 2002
- Attachment C** E-mail communication from (b) (6) (b) (6) dated July 19, 2002

This PMA Amendment is intended only to provide the e-mails in a formal submission for the record; this Amendment does not include any additional or revised information to what was provided in the e-mails. If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)

Printed by: (b) (6)
Title: Tubal ligation/device removal subsequent to Essure placement

Thursday, September 12, 2002 2:58:28 PM
Page 1 of 1



Sunday, July 14, 2002 11:49:33 AM

Message

From: (b) (6)

Subject: Tubal ligation/device removal subsequent to Essure placement

To: (b) (6)

Cc: (b) (6)

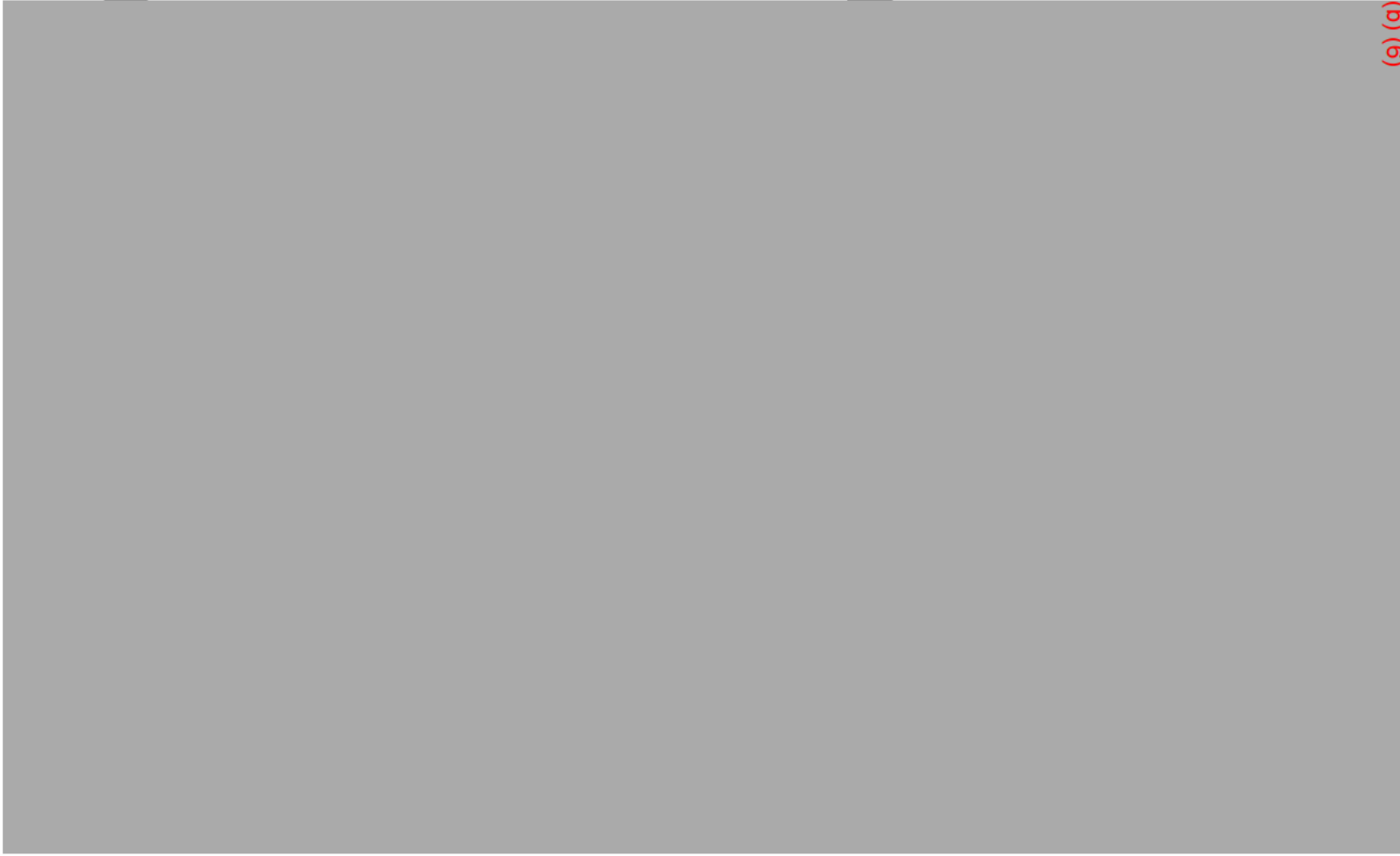
Attachments: Tubal ligation, Device removal 16K

Attached is a table that was prepared to respond to your phone inquiry of Friday, July 12, 2002 regarding device removals. (b) (6) and I tried to reach you several times today (Sunday) by phone, per your request, but were unable to reach you. So, we decided to send the information by e-mail instead. If the attached is not self-explanatory, then we can speak tomorrow. I will fax a copy of the attachment as well, in case there is any trouble opening the attachment.

P.S. Hope you didn't lose too much of your weekend to the panel preparations!

(b) (6)


(b) (6)



u

Printed by: (b) (6)
Title: **Response to (b) (6) questions of July 8, 2002**

Friday, September 13, 2002 10:24:22 AM
Page 1 of 1

 Wednesday, July 17, 2002 6:42:05 PM
Urgent Message

From:  (b) (6)

Subject: Response to (b) (6) questions of July 8, 2002

To: (b) (6)

Cc:

Attachments:  (b) (6) ~1.DOC 294K

Attached is our response to the questions raised by (b) (6), as forwarded in an e-mail from (b) (6) on July 8, 2002. We apologize for the 2-day delay in the requested response time. Our delay was due to the simultaneous QSIT and BIMO audits from the FDA that we hosted last week, as well as the requirement to provide a clinical update in a PMA Amendment on July 15, 2002.

Please let me know if you have any questions regarding our response. We are available for a conference call tomorrow if necessary for (b) (6) to finalize his panel presentation.

(b) (6)

(b) (4)



P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



* Rothman KJ, Greenland S. *Modern Epidemiology*. Philadelphia, PA: Lippincott-Raven, 1998:xiii, 737.

† According to the protocol and statistical analysis plan approved under IDE G000055, the recruitment goal in the Pivotal trial was to enroll approximately 1/3 “older” women (age 34 and above) and 2/3 “younger” women (age < 34), not to enroll based on three age group categories.

PG20014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



P020014. Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

7

(b) (4)



P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

8

(b) (4)



July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



FD-2001-E Response to July 8, 2002 Questions from

(b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



(b) (6)



FO 0014 Response to July 8, 2002 Questions from

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



(b) (6)



FD-20014 Response to July 8, 2002 Questions from

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



‡ The figure is less than $17 \times 12 = 204$ since some women were lost to follow-up after the 3-month or 6-month PAC visit.

P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (6)



(b) (6)

P020014 Response to July 8, 2002 Questions from

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



PO20014 Response to July 8, 2002 Questions from

(b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



1000014 Response to July 8, 2002 Questions from

(b) (6)



July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



P020014 Response to July 8, 2002 Questions from

(b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

19

(b) (4)



§ Taffe J, and Dennerstein L. Retrospective self-report compared with menstrual diary data prospectively kept during the menopausal transition. *Climacteric* 2000;3:183-191.

P020014. Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

20

(b) (4)



P020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

21

(b) (4)



P020014 Response to July 8, 2002 Questions from

(b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



PO20014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

APPENDIX A

(b) (4)



** Rothman KJ. *Modern Epidemiology*. 1986 Little Brown and Co. Boston/Toronto, Chapter 5.
16020014 Response to July 8, 2002 Questions from (b) (6)

July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

APPENDIX B

(b) (4)



P020014 Response to July 8, 2002 Questions from

(b) (6)



July 17, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (6)

From: (b) (6)
Sent: Friday, July 19, 2002 2:24 PM
Cc: (b) (6)
Subject: Phase II data



Note2 to Dr
(b) (6).doc

(b) (6)
(b) (4)

(b) (6)

(b) (6)

(b) (6), (b) (4)



P020014/AM

Conceptus, Inc.

Conceptus.

September 20, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED
SEP 23 10 25 AM '02
FDA/CDRH/OCE/DHC

Re: Amendment to PMA No. P020014
Response to Questions from (b) (6) email received 9/19/02
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

Conceptus Inc. is hereby submitting its response to questions from (b) (6) email received 9/19/02. FDA questions are repeated below in italics with Conceptus' response following.

(b) (4)



Conceptus, Inc.

(b) (6)



If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)



PMA Amendment
September 20, 2002

Confidential

Page 2 of 2

2

Conceptus, Inc.

Conceptus.

September 20, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED

SEP 23 10 25 AM '02

FDA/CDRH/OCE/DMC

Re: Amendment to PMA No. P020014
Response to Questions from (b) (6) email received 9/19/02
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

Conceptus Inc. is hereby submitting its response to questions from (b) (6) email received 9/19/02. FDA questions are repeated below in italics with Conceptus' response following.

(b) (4)



3

Conceptus, Inc.

(b) (6)



If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)



PMA Amendment
September 20, 2002

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Page 2 of 2

4

P020014 A15

Conceptus.

RECEIVED
SEP 23 10 37 AM '02
FOIA/CDRH/4127/DMD

September 19, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Amendment to PMA No. P020014
Proposed Post-Market Surveillance Plans
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

This PMA Amendment is being provided to the Agency in response to its questions of August 6, 2002, September 12, 2002, and September 17, 2002 regarding post-market surveillance for the Essure System.

(b) (4)

SP-8

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(b) (4)



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(b) (4)



(b) (4)



(b) (4)



(b) (4)



¹ Macro downloadable at <http://ftp.sas.com/techsup/download/stat/glmm800.sas>. Examples available at <http://ftp.sas.com/techsup/download/stat/glmm800e.html>

PMA Amendment: Post-Market Surveillance
Response to Agency questions of 8/6/02, 9/12/02 and 9/17/02
P020014

Page 7 of 10

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

(b) (4)



(b) (4)



We hope that the responses provided herein have adequately addressed your requests. Please let me know if you have any questions. I can be reached at (b) (6), or by fax at (b) (6), or by e-mail at (b) (6). In addition, you may contact (b) (6), by fax at (b) (6), or by e-mail at (b) (6). Thank you for your continued review of this PMA application.

Sincerely,

(b) (6)

A large rectangular area of the document is redacted with a solid grey fill, obscuring the signature and any handwritten notes.

Attachments: Exhibit A and B

**Post-Market Surveillance of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials**

(IDEs: G980152 and G000055)

**Conceptus Research Protocol
Essure 5-Year**

**Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070
U.S.A.**

Telephone: (b) (6)

Fax: (650) 610-8363

REVISION HISTORY

Original Protocol, Rev 00

9/19/02

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2. Purpose of Study	4
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6. Investigators and Qualifications	5
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1. TITLE

“Post-Market Surveillance of the Essure System: 5 Year Follow-up under Phase II and Pivotal Trials.”

2. PURPOSE OF STUDY

The purpose of this study is to demonstrate the long-term safety and effectiveness of Essure in providing permanent contraception.

3. STUDY DESIGN

This protocol combines the long-term follow-up already planned under the Phase II (Conceptus protocols #STOP 07/10; IDE #G980152) and Pivotal trials (Conceptus protocol #STOP 2000; IDE #G000055). Specifically, study participants implanted with at least one Essure Micro-insert will be followed annually for 5 years.

Findings from the U.S. Collaborative Review of Sterilization (CREST¹ study) will be used as a qualitative assessment.

Reference

1. Peterson HB, Xia Z, Hughes JM, et al. The risk of pregnancy after tubal sterilization: Findings from the U.S Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-1170

4. STUDY PLAN

Study participants who received implantation with at least one Essure Micro-insert in the Phase II or Pivotal trials of the Essure System (gamma design) will be followed for 5 years. Participants who are not relying on Essure for contraception will be followed for safety evaluation only, at 2, 3, 4, and 5 years after implantation. Participants who are relying on Essure for contraception will be followed for safety and effectiveness evaluation at 2, 3, 4, and 5 years after discontinuation of alternative contraception. The Pivotal trial and Phase II protocols also include an 18 month follow-up visit for study participants who are relying on Essure for contraception. However, since this post-market surveillance protocol is intended to provide *annual* effectiveness rate information, the 18-month visit will not be included in this protocol. The data from the 18-month visit will instead be reported in the IDE annual progress reports. Participants terminated from the Phase II or Pivotal trial due to lack of Micro-insert placement,

Micro-insert explantation, or who have become lost-to-follow-up in those studies, will not be followed under this protocol.

5. PRIMARY AND SECONDARY ENDPOINTS

5.1 The primary endpoints for the study are as follows:

1. Prevention of pregnancy for 5 years,
2. Safety of device wearing for 5 years

Pregnancy prevention will be determined by a pregnancy test at the 2 and 5 year follow-up visits and by phone assessment at the 3 and 4 year follow-up visits. Safety of device wearing will be evaluated by recording adverse events at each of the scheduled follow-up visits.

5.2 The secondary endpoint for the study are as follows:

1. Participant satisfaction with device wearing for 5 years,

Participant satisfaction with device wearing will be evaluated by participant interviews at scheduled follow-up visits.

6. INVESTIGATORS AND QUALIFICATIONS

The Investigators who participated in the Phase II and Pivotal trials will be the same Investigators who participate under this post-market surveillance protocol.

7. STUDY POPULATION

Study participants will be women who received implantation of at least one Essure Micro-insert in the Pivotal trial and participants in the Phase II trial that received at least one Micro-insert and agreed to be followed for 5 years¹.

(b) (4)



This study will not include those women terminated from the Phase II or Pivotal trials.

8. STUDY PROCEDURES

The case report forms for this study are included in **Appendix B**, and are the same as currently used in the Phase II and Pivotal trials.

All study procedures will be paid for by the Sponsor.

9.1 Follow-up Visits and Phone Contact

A description of each visit and phone contact is provided below.

9.1.1 Phone contact will be scheduled at three and four years following discontinuation of alternative contraception.

9.1.2 Office visits will be scheduled two and five years following discontinuation of alternative contraception.

9.1.3 Any participant who has had one or more Essure devices implanted, but is not able to rely on the device(s) for contraception, for any reason, will be followed at the 2, 3, 4 and 5 year follow-up time points (post-device placement) for safety and participant tolerance to device wearing. This includes participants who have had incisional sterilization, subsequent to Essure Micro-insert placement but without Micro-insert removal.

9.1.4 Additional office visits required for the investigation or management of an adverse event(s) must be recorded on the "Unscheduled Visit" Case Report Form.

9.2 Three-, Four-Year *Post-Discontinuation of Alternative Contraception*

Follow-Up Phone Contact

9.2.1 Three years and four years (plus or minus four weeks) following discontinuation of alternative contraception, the Investigator or

designee will contact the participant to discuss her well-being and to confirm that the participant does not suspect that she is pregnant. The Investigator or designee will discuss any unusual pain or bleeding experienced by the participant, any late menses, or any other unusual symptoms.

9.2.2 If pelvic infection is suspected, the participant will be instructed to return to the Investigator's office and a culture should be taken before administering antibiotics.

9.2.3 If device migration, expulsion or unsatisfactory device location is suspected, refer to "Protocol for Management of Potential Device Movement or Unsatisfactory Device Location" (Appendix B).

9.2.4 The participant will be instructed to inform the Investigator:

9.2.4.1 if she is no longer sexually active (less than 4-8 coital acts per cycle):

9.2.4.2 if she has used any other method of contraception (including condoms, even if used only for STD protection);

9.2.4.3 if there have been any changes that would affect her or her partner's fertility;

9.2.4.4 if she has changed partners;

9.2.4.5 if she is scheduled to undergo any intrauterine procedure such as endometrial biopsy, D&C, or hysteroscopy (diagnostic or operative) including endometrial ablation or resection;

9.2.4.6 if she is scheduled to undergo any extirpative surgery of reproductive organs (hysterectomy, salpingectomy, oophorectomy).

9.2.5 The participant will be advised that she should use condoms whenever she thinks she might be at immediate risk for a sexually

transmitted disease. However, prolonged use of condoms or other forms of contraception will result in an inability for Conceptus to include this participant in the effectiveness data analysis. Prolonged use is defined as use during more than 50% of the coital acts (4-8 required per cycle) during two cycles, following the Investigator's instruction to discontinue contraception. Such a participant will be followed at the 2,3,4, and 5 year follow-up time points for safety and participant tolerance to device wearing.

9.2.6 The participant will be instructed to contact the Investigator immediately if, at any time during the study, she thinks she might be pregnant.

9.3 Two- and Five-Years *Post Discontinuation of Alternative Contraception* Follow-Up Visit

9.3.1 Two and five years (plus or minus 4 weeks) following discontinuation of alternative contraception, the participant will return to the Investigator's office for the following procedures:

9.3.1.1 A gynecological exam to evaluate any pelvic tenderness that may be associated with the device;

9.3.1.2 A speculum exam to assess cervical inflammation or infection;

9.3.1.3 A urine or serum pregnancy test to confirm that the participant is not pregnant;

9.3.1.4 A pelvic x-ray to determine device location. One copy of the x-ray will be retained at the Investigational site and two copies will be sent to Conceptus for the study files.

9.3.2 The Investigator will also discuss with the participant her well-being, any unusual pain or bleeding experienced by the participant, any late menses, or any other unusual symptoms.

- 9.3.3 If pelvic infection is suspected, a culture should be taken before administering antibiotics.
- 9.3.4 The participant will be instructed to inform the Investigator:
 - 9.3.4.1 if she is no longer sexually active (less than 4-8 coital acts per cycle);
 - 9.3.4.2 if she has used any other method of contraception (including condoms, even if used only for STD protection);
 - 9.3.4.3 if there have been any changes that would affect her or her partner's fertility;
 - 9.3.4.4 if she has changed partners;
 - 9.3.4.5 if she is scheduled to undergo any intrauterine procedure such as endometrial biopsy, D&C, or hysteroscopy (diagnostic or operative) including endometrial ablation or resection;
 - 9.3.4.6 if she is scheduled to undergo any extirpative surgery of reproductive organs (hysterectomy, salpingectomy, oophorectomy).
- 9.3.5 If device migration, expulsion or unsatisfactory device location is suspected, refer to "Protocol for Management of Potential Device Movement or Unsatisfactory Device Location" (Appendix B).
- 9.3.6 The participant will be advised that she should use condoms whenever she thinks she might be at immediate risk for a sexually transmitted disease. However, prolonged use of condoms or other forms of contraception will result in an inability for Conceptus to include this participant in the effectiveness data analysis. Prolonged use is defined as use during more than 50% of the coital acts (4-8 required per cycle) during two cycles, following the Investigator's instruction to discontinue contraception. Such a

participant will be followed at the 2,3,4, and 5 year follow-up time points for safety and participant tolerance to device wearing.

9.3.7 The participant will be instructed to contact the Investigator immediately if, at any time during the study, she thinks she might be pregnant.

9.4 Intrauterine Procedures Post-Essure Placement

Participants will be instructed to contact the Investigator if they are scheduled to undergo any intrauterine procedure such as endometrial biopsy, dilatation and curettage (D&C), or hysteroscopy (diagnostic or operative) including endometrial ablation or resection. If such a procedure(s) is scheduled, the Investigator should inform the physician who will be conducting the procedure that there may be risks associated with the presence of the Essure Micro-inserts that, at this time, have not been identified. In the event of a hysteroscopic procedure, the Investigator will request the physician to make an evaluation of the tissue surrounding any portion of the Essure Micro-insert trailing into the uterine cavity and to provide photos and video footage when possible.

9.5 Extirpative Surgery of Reproductive Organs Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any extirpative surgery of the reproductive organs (hysterectomy, salpingectomy, oophorectomy), *for any reason*, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes and provide photos and video footage when possible. In the event that the extirpative surgery occurs in a participant whose devices were known to be located in her peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the location of the device, a determination as to whether the device(s) were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s). The search for the device should be limited to 30 minutes, and any free-floating devices should be retrieved and returned to Conceptus. The Investigator should obtain the excised fallopian tubes, when possible, and send them to Conceptus for histological evaluation. In any case, histology specimens

retrieved should be evaluated and results forwarded to the Investigator and Conceptus. If the participant is scheduled to undergo any intrauterine sampling procedure (D&C, endometrial biopsy), histology results should also be forwarded to the Investigator and Conceptus.

9.6 Transabdominal Surgery Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any surgery in the peritoneal cavity that would permit visualization and evaluation of the fallopian tube exterior, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes, and provide photos and video footage when possible. In the event that the surgery occurs in a patient whose devices were known to be located in the peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the location of the device, a determination as to whether the devices were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s).

10 ADVERSE EVENTS

Adverse events are defined as any untoward deviations in subject health away from baseline. Investigators must record and document all adverse events in the case report form, and record and report any unanticipated device related adverse effects to Conceptus and the reviewing IRB / Ethics Committee as soon as possible but no longer than 5 working days after becoming aware of the event. Unanticipated adverse device effect means any serious adverse effect on health or safety, or any life-threatening problem or death caused by or associated with a device, *if* that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan *or* any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. For all serious adverse events, the Investigator will send to Conceptus all appropriate paperwork (discharge summaries, office notes, etc.) that might be pertinent.

11 RECORDS AND REPORTS

11.1 Each Investigator will maintain the following accurate, complete and current records relating to the Investigator's participation in an investigation:

11.1.1 All correspondence with another Investigator, an IRB or Ethics Committee, the sponsor, a monitor, or the FDA / other health authority, including required reports.

11.1.2 Records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

11.1.2.1 Documents evidencing informed consent.

11.1.2.2 All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

11.1.2.3 A record of the exposure of each subject to the Essure Micro-insert(s), including the date and time of each use, and any other therapy.

11.1.3 The protocol, with documents showing the dates of any reasons for any deviation from the protocol.

11.1.4 Any records that FDA or other health authority requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

11.2 The Investigator or designee will input the required study data into password protected, electronic case report forms that will be maintained on a website for the Pivotal trial participants.

11.2.1 Case Report Forms should be printed out after Conceptus monitoring and data queries have been completed for the specified form. Forms will be accessible to the Investigator, his or her authorized staff, and to representatives of the Sponsor for the purpose of monitoring the study and auditing the data and participant records. The United States Food and Drug Administration (FDA) or other health authority also may require access to the forms and participant records.

11.3 Phase II data will be collected on hard copy CRFs.

11.4 Participant identity will be kept confidential by assigning unique participant numbers to each participant. The medical record number for each participant will be recorded on a participant number log in order to allow traceability of each participant's records. Participant numbers and initials will be used to identify participants on case report forms. Participant names will not be kept with the data. Any publications or presentations that result from this study will maintain participant confidentiality.

11.5 Each Investigator shall prepare and submit the following complete, accurate and timely reports:

11.5.1 Unanticipated adverse device effects (please refer to section 10 of this protocol for reporting requirements).

11.5.2 Withdrawal of IRB or Ethics Committee approval. An Investigator shall report to Conceptus, within 5 working days, a withdrawal of approval by the reviewing IRB/Ethics Committee of the Investigator's part of an investigation.

11.5.3 An Investigator shall submit progress reports on the investigation to Conceptus, the monitor, and the reviewing IRB or Ethics

Committee at regular intervals, but in no event less often than yearly.

11.5.4 Deviations from the investigational plan. An Investigator shall notify Conceptus and the reviewing IRB or Ethics Committee of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by Conceptus is required for changes in or deviations from the protocol, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, approval from the FDA or other health authority and the IRB/Ethics Committee also is required.

11.5.5 Informed consent. If an Investigator uses a device without obtaining informed consent, the Investigator shall report such use to Conceptus and the reviewing IRB or Ethics Committee within 5 working days after the use occurs.

11.5.6 An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB or Ethics Committee.

11.5.7 An Investigator shall, upon request by a reviewing IRB or Ethics Committee, FDA or other health authority, provide accurate, complete and current information about any aspect of the investigation.

11.6 Each Investigator will maintain all study-related records during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a pre-market approval application (PMA) or a notice of completion of a product development protocol.

12 ANALYSIS AND REPORTING OF RESULTS

12.1 The data from this post-market surveillance study will be analyzed according to the statistical analysis plan attached as **Appendix A**.

13 RISKS

The risks of study participation were outlined in the protocols and consent forms approved by the FDA and the overseeing IRBs/Ethics Committees for the Phase II and Pivotal trials. No new risks were identified in the clinical trials of Essure.

13 FINANCIAL ISSUES

(b) (4)



(b) (4)



15. DATE OF COMMENCEMENT

The proposed date of commencement for this post-market surveillance plan is immediately upon PMA approval.

Appendix A
STATISTICAL ANALYSIS PLAN

Post-Market Surveillance of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials
(IDEs: G980152 and G000055)

Conceptus Research Protocol
Essure 5-Year

(b) (4)



³ <http://www.mrc-bsu.cam.ac.uk/bugs/welcome.shtml>

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(b) (4)



⁴ Calculations performed with Hintze, J (2001). NCSS and PASS. Number Cruncher Statistical Systems. Kaysville, UT. <http://www.ncss.com>

Figure 1

(b) (4)



Appendix B

Case Report Forms

Essure™ System
US Postmarket Surveillance Plan for Newly Trained Physicians

DRAFT

September 19, 2002

Conceptus Protocol
Essure PMS Placement

Sponsor:

Conceptus Incorporated

1021 Howard Avenue

San Carlos, CA 94070

Telephone 650-628-4700

Fax 650-802-2890

REVISION HISTORY (to be started after final version is approved by FDA)

LDC

PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A016 PANEL OB DIVISION DRARD BRANCH OGDB
 TRADE NAME ESSURE SYSTEM
 GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE
 PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.
 SHORT NAME CONCEPTUS
 CONTACT (b) (6)
 DIVISION _____
 ADDRESS 1021 HOWARD AVE.
SAN CARLOS, CA 94070
 PHONE NO. (b) (6) FAX NO. (650) 610-8363
 MANUFACTURER CONCEPTUS, INC. REG NO. 2951250
(b) (4) (b) (4)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 26-SEP-2002 CYCLE # 1
 DATE RECEIVED IN ODE 27-SEP-2002 CYCLE START 22-APR-2002
 DATE FILING DUE _____ ELAPSED _____ LAST CYCLE _____
 DATE DECISION DUE _____ FDA TIME 158 _____ 158
 MFR TIME 0 _____ 0

AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
C001	FILE	22-APR-2002	
A001	UMIN	03-MAY-2002	
A002	UMIN	16-MAY-2002	
A003	UMIN	28-MAY-2002	
A004	UMIN	07-JUN-2002	
A005	UMIN	13-JUN-2002	
A006	UMIN	24-JUN-2002	
A007	UMIN	24-JUN-2002	
A008	UMIN	18-JUL-2002	
A009	UMIN	21-AUG-2002	
A010	UMIN	21-AUG-2002	
A011	UMIN	23-AUG-2002	
A012	UMIN	04-SEP-2002	
A013	UMIN	16-SEP-2002	
A014	UMIN	23-SEP-2002	
A015	UMIN	23-SEP-2002	

PO20014/A16

DRAERD REVIEWER RECORD FOR ORIGINAL SUBS,
AND PMA AND IDE SUPPLEMENTS

Document No. _____ Reviewer _____ Date Assigned _____

CONSULTING REVIEWS DESIGNATED, AS APPROPRIATE, BY BRANCH CHIEF AND LEAD REVIEWER, AT THE BEGINNING OF THE REVIEW:

<u>SPECIALTY</u>	<u>REVIEW NEEDED?</u>		<u>REVIEWER</u>	<u>DATES</u>	
	YES	NO		SENT	RETURNED
CLINICAL	_____	_____	_____	_____	_____
ENGINEERING/ PHYSICS	_____	_____	_____	_____	_____
CHEMISTRY/ BIOMATERIALS	_____	_____	_____	_____	_____
SOFTWARE	_____	_____	_____	_____	_____
IMMUNOLOGICAL/ STERILITY	_____	_____	_____	_____	_____
TOXICOLOGY/ BIOCOMPATIBILITY	_____	_____	_____	_____	_____
STATISTICS	_____	_____	_____	_____	_____
OTHER _____	_____	_____	_____	_____	_____

COMMENTS:

REVISED 1/7/96 LMS
 ON LAN AS REVREC.FRM

QUALITY CONTROL OVERVIEW OF DOCUMENT

A. ASSOC. DIRECTOR QC OVERVIEW: MEDICAL QC OF SUBMISSION IS NECESSARY?

YES _____ NO _____ INITIALS/DATE _____

B. IF YES IS NOTED ABOVE, MEDICAL OFFICER QC OVERVIEW:

1. Examination of the specialty reviews indicate there are remaining clinical issues that should be addressed (See attached sheet for summary).

INITIALS/DATE _____

2. In my opinion, all pertinent clinical issues have been adequately addressed.

FINAL SIGNOFF: MEDICAL OFFICER/DATE _____

FINAL SIGNOFF: ASSOC. DIRECTOR/DATE _____

REVISED: 1/2/96 LMS
LOCATED ON LAN AS REVREC.FRM

P020014/A16

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

September 27, 2002

(b) (6)
CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A016
Dated: 26-SEP-2002
Received: 27-SEP-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (301)594-5072. All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours

(b) (6)

Center for Devices and
Radiological Health

P020014/A16

Conceptus, Inc.

Conceptus®

September 26, 2002

RECEIVED
2002 SEP 27 A 10:19
FDA/CDRH/OCE/PMO

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: Amendment to PMA No. P020014
Formal Amendment to respond to (b) (6) question on (b) (4)
Rate (email dated 9/20/02)
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

Conceptus Inc. is submitting this PMA Amendment to formalize its response to Dr. (b) (6) (b) (6) question (email dated 9/20/02) concerning (b) (4) rate (Question #1). This response was provided to (b) (6) and (b) (6) via email on September 20, 2002.

Below is a brief summary of the communication in this regard:

Summary

(b) (4), (b) (6)



Conceptus, Inc.

(b) (4)

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If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, and at (b) (6) via e-mail.

Sincerely,

(b) (6)

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Conceptus, Inc.

Conceptus.

P02 0014/A17

September 27, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED
2002 SEP 30 A 11:35
FDA/CDRH/OCE/PMO

Re: Amendment to PMA No. P020014
Response to FDA Questions sent via email on 9/17/02
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6):

Conceptus Inc. is hereby submitting its response to the FDA's questions communicated via email on September 17, 2002. FDA's questions are repeated below in italics, followed by our response in plain text. A brief background regarding the communication history is provided first.

Background

Questions from the Agency were first received on August 6, 2002 via e-mail. In response to those questions the following was submitted by Conceptus:

1. Formal PMA Amendment dated August 20, 2002 regarding Engineering, Corrosion and Shelf Life questions (Response to Questions #1-3 under the headings "Engineering", Questions #4-6 "Corrosion" and Questions #7-9 "Shelf Life").
2. Informal Draft PMA Amendment dated August 21, 2002 regarding Clinical and Labeling questions (Response to Questions #11-17 under the heading "Clinical", Question #12 under the heading "MRI" and Question #13 under the heading "Labeling").
3. Informal Draft PMA Amendment dated August 26, 2002 regarding Post-Market Surveillance, followed by a formal PMA Amendment regarding Post-Market Surveillance which addressed FDA's comments (dated 9/12/02 and 9/17/02) regarding our August 26, 2002 draft PMA amendment.

Conceptus, Inc.

This PMA Amendment is intended to provide a response to the questions raised in FDA's e-mail communication of September 12, 2002, which was in response to our draft PMA Amendment dated August 21, 2002 (referenced in # 2 above).

Communication Summary Relevant to this Amendment

- August 6, 2002 – FDA Questions Received (e-mail)
- August 21, 2002 – Draft Response Provided to FDA (e-mail) [Questions #11-17, #12, #13]
- September 12, 2002 – FDA Questions Regarding 8/21/02 draft Response Received (e-mail)

FDA Questions and Conceptus Response

(b)(4)



(b)(4)



¹ Rock JA, Parmley TH, King TM, Laufe LE, Su BS. Endometriosis and the development of tuboperitoneal fistulas after tubal ligation. *Fertil Steril.* 1981;35:16-20.

² Surgical Implants and Other foreign Bodies, chapter 6 Summary of Data Reported and Evaluation, IARC, vol. 74 (1999).

³ Klosterhalfen B, Klinge U, Hermanns B, Schumpelick V. [Pathology of traditional surgical nets for hernia repair after long-term implantation in humans]. *Chirurg.* 2000;71:43-51.

(b)(4)



¹ Rock JA, Parmley TH, King TM, Lafe LE, Su BS. Endometriosis and the development of tuboperitoneal fistulas after tubal ligation. *Fertil Steril*. 1981;35:16-20.

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Conceptus, Inc.

(b)(4)

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Sincerely,

(b) (6)

A rectangular area below the signature line is redacted with a solid grey fill, obscuring the name and any handwritten notes.

Enclosures:

- **Exhibit A – Exhibit F**
- Reference Articles

References:

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EXHIBIT A

Long term tissue responses to Essure

(b)(4)



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Human mast cells stimulate fibroblast proliferation, collagen synthesis and lattice contraction: a direct role for mast cells in skin fibrosis

E. Garbuzenko, A. Nagler*, D. Pickholtz, P. Gillery†, R. Reich, F.-X. Maquart† and F. Levi-Schaffer

Department of Pharmacology, School of Pharmacy, Faculty of Medicine, The Hebrew University-Hadassah Medical School, *Department of Bone Marrow Transplantation, Hadassah University Hospital, Jerusalem, Israel, and †Laboratory of Biochemistry, UPRESA-CNRS 6021, IFR53 Biomolecules, Faculty of Medicine, Reims, France

Summary

Background Mast cells, the key cells of immediate hypersensitivity type reactions, have also been postulated to have a central role in influencing tissue remodelling and fibrosis occurring in the skin.

Objective Our aim was to investigate the direct role of human mast cells (HMC) in skin fibrotic processes, by assessing the effects of the addition of the human mast cell line HMC-1 to human skin fibroblasts, and to identify the responsible mediators.

Methods HMC-1 sonicates were added to human skin fibroblasts and the following parameters were evaluated: proliferation (^3H -thymidine), collagen synthesis (^3H proline), activity of matrix metalloproteinases (MMPs) (zymography) and tissue inhibitors of metalloproteinases (TIMPs) (reverse zymography), and collagen gel contraction.

Results HMC-1 sonicate increased significantly both proliferation and collagen production in the human skin fibroblasts and these properties were not affected by heating of the sonicate (56°C, 30 min, or 100°C, 3 min). Two main mast cell mediators, histamine and tryptase, were found to be responsible for the increase in fibroblast proliferation and collagen production. HMC-1 sonicate did not display any pre-formed gelatinase activity, and its addition to the fibroblasts did not change their pro-MMP-2 and MMP-2 activity. On the other hand, HMC-1 were found to possess TIMP-1 and TIMP-2. Addition of HMC-1 had no effect on fibroblasts TIMP-1 but induced a dose-dependent increase of TIMP-2 activity. In addition, HMC-1 sonicate seeded together with the fibroblasts in two-dimensional collagen gel significantly enhanced their contraction.

Conclusion We have shown that human mast cells, by granule-stored and therefore quickly releasable mediators, increase human skin fibroblast proliferation, collagen synthesis, TIMP-2 and collagen gel contraction. Therefore, mast cells have a direct and potentiating role in skin remodelling and fibrosis.

Keywords collagen gel, collagen, fibroblasts, fibrosis, human, mast cells, MMPs, proliferation, skin, TIMPs

Submitted 12 March 2001; revised 2 June 2001, accepted 1 August 2001

(b)(4)-Copyrighted Material

(b)(4)-Copyrighted Material

Acknowledgements

This work was partially funded by the Aimwell Charitable Trust (UK), CNRS and the University of Reims-Champagne-Ardenne. We gratefully acknowledge the technical assistance of Anne Rubin. F. Levi-Schaffer is affiliated with the David R. Bloom Center for Pharmacy at The Hebrew University of Jerusalem.

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Effect of activated human mast cells and mast cell-derived mediators on proliferation, type I collagen production and glycosaminoglycans synthesis by human dermal fibroblasts

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RESUME / SUMMARY

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Mots clés

Although an increased number of mast cells in fibrotic tissues such as scleroderma, keloid or healing wound has been highlighted, it is still unclear whether or not mast cells are fibrogenic. The aim of the present study is to determine whether functionally active human mast cells can provide human dermal fibroblasts directly with fibrogenic properties. In order to examine the effects of IgE-mediated mast cell activation on fibroblast proliferation and synthesis of type I collagen, we utilized an *in vitro* defined system in which cultured human mast cells were co-cultured with human dermal fibroblasts. We also employed a three-dimensional fibroblast culture system using supplementation of L-ascorbic acid as an assay system to investigate the effects of mast cell-derived mediators on synthesis of glycosaminoglycans by human fibroblast. Fibroblast proliferation was actively stimulated with IgE-activated mast cells. However, this stimulatory effect was canceled in co-cultures with a higher number of IgE-activated mast cells. In the presence of a higher number of activated mast cells, the fibroblast cell layer was destroyed, in contrast to an intact cell layer in the presence of same number of the mast cells without activation. Type I collagen synthesis was unchanged in fibroblasts co-cultured with mast cells. The total amount of main disaccharide units, particularly DELTADi-HA, was increased when fibroblasts were exposed to histamine. Thus, we conclude that other factors, in addition to mast cells, are important in the development of human tissue fibrosis or sclerosis.

Key-words *fibroblast, glycosaminoglycan, human cultured mast cell, three-dimensional culture system, scleroderma, skin fibrosis.*

ARTICLE

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Effect of activated human mast cells and mast cell-derived mediators on proliferation, type I collagen production and glycosaminoglycans synthesis by human dermal fibroblasts

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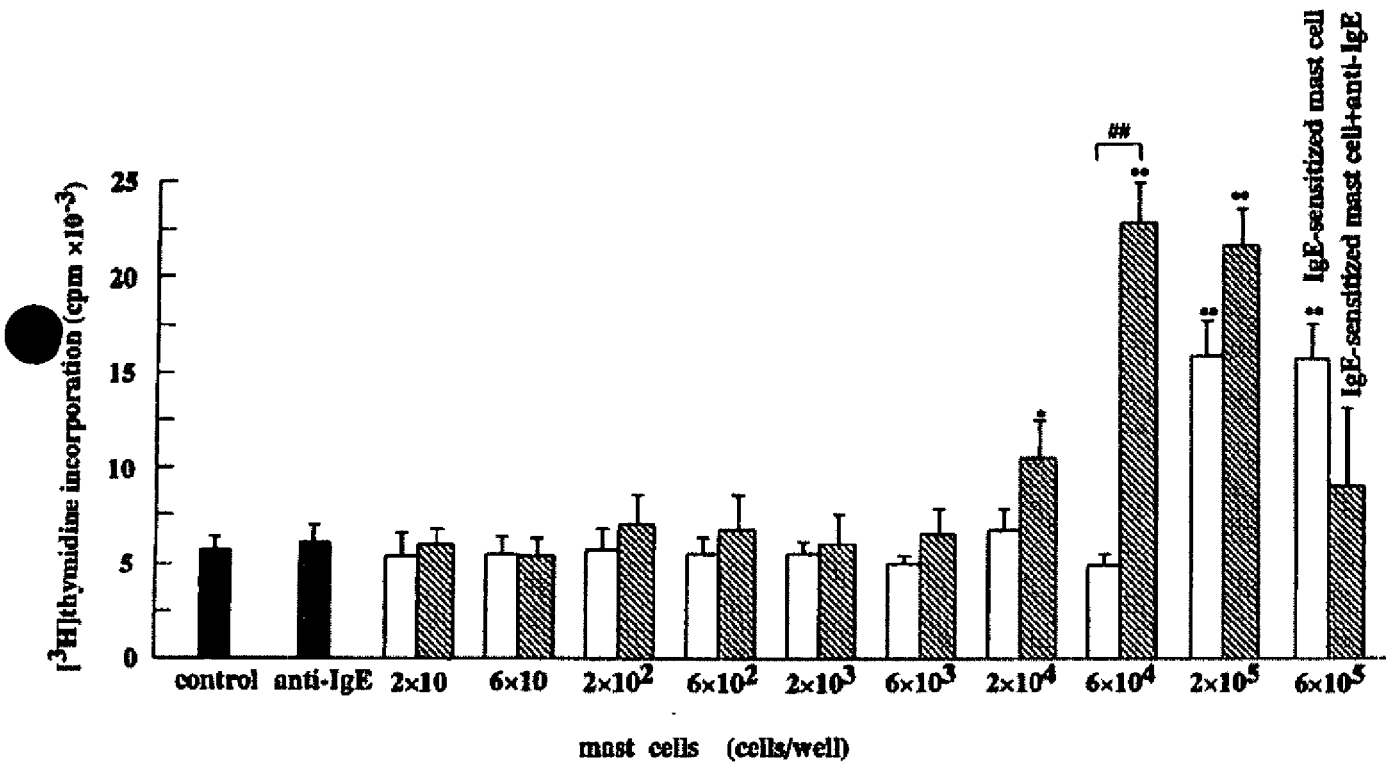


Figure 1. Proliferative response of human fibroblasts obtained by the explant culture technique co-cultured with human mast cells. Mast cells were sensitized with IgE and seeded onto confluent monolayers of fibroblasts. The proliferative response was measured using [³H]thymidine incorporation. The incorporation in fibroblasts incubated with medium alone (control), in the presence of anti-IgE (dotted bar) or with IgE-sensitized mast cells in the absence (open bar) or presence (shaded bar) of anti-IgE was investigated in five fibroblasts strains as described in the text. Values shown are means ± SEM. **p* < 0.05 and ***p* < 0.01, significant difference from the control. ##*P* < 0.01, significant difference from group indicated.

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ENDOMETRIOSIS AND THE DEVELOPMENT OF TUBOPERITONEAL FISTULAS AFTER TUBAL LIGATION*

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The present study details gross and histologic findings of 79 previously ligated fallopian tubes from 3 groups of patients. Of 20 oviducts removed after documented sterilization failure (group I), 6 revealed a process compatible with endometriosis. Four of nine previously ligated fallopian tubes removed at the Johns Hopkins Hospital (group II) were successfully injected with India ink. In two patients histologic examination demonstrated the India ink in epithelium-lined spaces that lay beyond the muscle of the tubal wall extending from the tubal lumen to the serosal surface.

Fifty oviducts were studied in twenty-five patients requesting reversal of their sterilizations (group III). A higher percentage of fistulas was demonstrated in patients with less than 4 cm of remaining proximal tubal segment. Furthermore, most of these fistulas were demonstrated in patients for whom 3 years had elapsed since the original sterilization procedure. Patients sterilized by laparoscopic cautery methods were observed to have a higher percentage of fistula formation and histologic documentation of endometriosis at the sterilization site as compared with patients sterilized by other methods. Our observations suggest that ligation of the oviduct within 4 cm of the uterine cornu may predispose to the development of endometriosis and subsequent fistula formation in the tip of the ligated oviduct.
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SURGICAL IMPLANTS AND OTHER FOREIGN BODIES

VOL.: 74 (1999)

6. Summary of Data Reported and Evaluation

6.1 Exposure data

A wide range of metals and their alloys, polymers, ceramics and composites are used in surgically implanted medical devices and prostheses and dental materials. Most implanted devices are constructed of more than one kind of material (implants of complex composition). Since the early 1900s, metal alloys have been developed for these applications to provide improved physical and chemical properties, such as strength, durability and corrosion resistance. Major classes of metals used in medical devices and dental materials include stainless steels, cobalt-chromium alloys and titanium (as alloys and unalloyed). In addition, dental casting alloys are based on precious metals (gold, platinum, palladium or silver), nickel and copper and may in some cases contain smaller amounts of many other elements, added to improve the alloys' properties.

Orthopaedic applications of metal alloys include arthroplasty, osteosynthesis and in spinal and maxillofacial devices. Metallic alloys are also used for components of prosthetic heart valve replacements, and pacemaker casings and leads. Small metallic parts may be used in a wide range of other implants, including skin and wound staples, vascular endoprostheses, filters and occluders. Dental applications of metals and alloys include fillings, prosthetic devices (crowns, bridges, removable prostheses), dental implants and orthodontic appliances.

Polymers of many types are used in implanted medical devices and dental materials. Illustrative examples are silicones (breast prostheses, pacemaker leads), polyurethanes (pacemaker components), polymethacrylates (dental prostheses, bone cements), poly(ethylene terephthalate) (vascular grafts, heart valve sewing rings, sutures), polypropylene (sutures), polyethylene (prosthetic joint components), polytetrafluoroethylene (vascular prostheses), polyamides (sutures) and polylactides and poly(glycolic acids) (bioresorbables).

Ceramic materials based on metal oxides (alumina, zirconia) find use in joint replacements and dental prostheses. Other materials based on calcium phosphate are used as bone fillers and implant coatings. Pyrolytic carbon applications include heart valves and coatings for implants. Composites are used mainly in dental fillings.

Although precise numbers are not available, many millions of people worldwide have implanted devices, which may remain in place for years.

Foreign bodies, such as bullets and pellets from firearms and metallic fragments from explosions, may penetrate and remain in human tissues for long periods of time. Internal exposure to constituents, including lead (from bullets and pellets) and depleted uranium (from shell and missile fragments), may result.

6.2 Human carcinogenicity data

Sixteen case reports have described neoplasms originating from bone or soft connective tissue in the region of metal implants. An analytical study did not report an increased risk for soft-tissue sarcoma after metal implants. No association with dental amalgam was found in a case-control study in Australia.

The 30 case reports of breast cancer following silicone implants for cosmetic breast augmentation appear unlikely to correspond to an excess of breast cancer. All five cohort studies involving a total of more than 18,000 women treated with surgical prostheses made of silicone (or polyurethane-coated silicone) for cosmetic breast augmentation conducted in Canada, Denmark, Sweden and the United States consistently found no evidence of increased risk of breast cancer. The combined results of the four largest cohort studies show a 25% reduction in risk. Similar results were reported by a large case-control study including more than 2000 cases and 2000 controls in the United States. All cohort studies were based on subjects exposed to implanted silicone at an early age, usually between the ages of 30 and 40 years, so that the number of breast cancer cases observed in each study was relatively small. Except for the case-control study in the United States, only limited allowance was made for potential confounding factors, although no clear evidence has emerged as to the relevance of any such factor to a possible association between implanted silicone and breast cancer risk.

Three of the studies considered the issue of latency, with observation periods of up to 10 years or more, but even in the group of women with follow-up of 10 years or more, there was no suggestion of increased risk. The risk of cancer following surgical implantation of silicone prostheses for breast reconstruction after breast cancer was considered in a study in France. The results of this study suggest no excess risk of second primary breast or other cancer, distant metastases, local recurrence or death from breast cancer. The reduced risks for breast cancer found in the cohort and case-control studies are unlikely to be due to chance, and no bias that would explain these findings has been identified. Four cohort studies of women with surgical breast implants in Denmark, Sweden and the United States reported on cancers at sites other than the breast. None of these studies found an increased risk for all cancers combined. Two studies reported increased risk for lung cancer, but these results were based on a total of only nine observed cases. For no other cancer site was there consistent evidence of an increased risk, although the statistical power to detect an increased risk of rare neoplasms, including soft-tissue sarcomas, was small.

Out of the large number of patients with orthopaedic implants of complex composition (metal with bone cement with or without polyethylene), a total of 35 cases have been reported of malignant neoplasms arising from the bone or the soft tissue in the region of an implant. Fourteen cohort studies of patients following total knee or total hip replacement from six countries were performed to investigate cancer incidence in these populations. Two of the studies from Finland and two studies from Sweden were partially overlapping. One study included only patients with metal-on-metal implants, five studies included only patients with polyethylene-on-metal implants, while the remaining studies included patients with mixed or unspecified types of implant. One study showed a small increase in overall cancer incidence, while the remaining studies showed overall decreases. Four of these studies suggested an excess risk for specific cancers, including Hodgkin's disease, non-Hodgkin lymphoma, leukaemia and kidney cancer. However, results of the other studies were not consistent with this observation. In one small cohort study from Denmark of patients with a finger or hand implant, an increased risk of lymphohaematopoietic cancer was observed. Additionally, two case-control studies, one including cases with soft-tissue sarcoma and the other including lymphoma and leukaemia, were carried out in the United States. The latter overlaps with one of the cohort studies. Neither of these studies showed an association with the presence of implants of complex composition. Most of the studies did not have information on possible confounding variables such as immunosuppressive therapy or rheumatoid arthritis for the lymphomas and analgesic drugs for kidney cancer. The follow-up in most of the studies may have been too short to evaluate cancer occurring many years after exposure; in some studies with longer follow-up, the numbers of long-term survivors were low.

Thirteen cases of breast cancer and one case of plasmacytoma have been reported in patients with cardiac pacemakers. Ten cases of different neoplasms have been reported at the site of non-metallic foreign bodies. Eight cases of sarcoma have been reported at the site of vascular grafts. No conclusions

can be drawn from these case reports.

Twenty-three cases of sarcomas, twenty-three cases of carcinomas and seven cases of brain tumours have been reported at the site of metallic foreign bodies, mainly bullets and shrapnel fragments.

6.3 Veterinary studies

Despite the large number and variety of both metallic and non-metallic internal fixation devices used in dogs in recent decades, only about 60 cases of sarcomas, primarily of bone, have been reported. In addition, four cases of sarcomas at the site of other foreign bodies have been reported in dogs. One case-control study found no association between metallic implants used to stabilize fractures in dogs and the development of bone or soft-tissue tumours.

In contrast, at least 563 cases of vaccine-associated sarcomas in cats have been reported in just six years, with an estimated annual incidence of 1–13 per 10 000 vaccinated cats. Vaccine-associated sarcomas have been mostly associated with administration of recently introduced feline vaccines containing adjuvant. Tumours that develop at vaccination sites are morphologically different from those that develop at non-vaccination sites. A cohort study found that cats developed sarcomas in a shorter time at sites used for vaccination than at non-vaccination sites and that there was an increased risk for sarcoma development with increased numbers of vaccines at a given site.

6.4 Animal carcinogenicity data

Chromium metal powder was tested in rats by intramuscular and intrarenal administration, in mice and rats by intrapleural and intraperitoneal administration, in rats and rabbits by intraosseous implantation and in mice, rats and rabbits by intravenous injection. No increase in tumour incidence was observed in these studies, although most studies had limitations in design, duration or reporting.

Cobalt metal powder was tested in rats by intramuscular or intrathoracic injection, producing sarcomas at the injection site. Studies in rats by intrarenal injection and in rabbits by intraosseous injection had limitations in design, duration or reporting.

Nickel metal powder was tested by inhalation exposure in mice, rats and guinea-pigs, by intratracheal instillation in rats and Syrian hamsters, by intramuscular injection in rats and hamsters and by intrapleural, intraperitoneal, intraosseous and intrarenal injection in rats. It was also tested by intravenous injection in mice and rats. Nickel metal pellets were tested by subcutaneous administration in rats. The studies by inhalation exposure were inadequate for an evaluation of carcinogenicity. After intratracheal instillation of nickel, significant numbers of squamous-cell carcinomas and adenocarcinomas of the lung were observed in rats; one adenocarcinoma of the lung was observed in hamsters. Intrapleural injections induced sarcomas in rats. Subcutaneous administration of nickel metal pellets induced sarcomas in rats; intramuscular injection of nickel powder induced sarcomas in rats and hamsters; and intraperitoneal injections induced local carcinomas, mesotheliomas and sarcomas in rats. No significant increase in the incidence of local kidney tumours in rats was seen following intrarenal injection. Studies by the intraosseous and intravenous routes were inadequate for evaluation.

Titanium metal was tested in rats by intramuscular implantation of rods and by intraosseous administration of powder, rods or wire. No local tumours occurred.

Most *nickel-based alloys* that have been tested for carcinogenicity in animals are not actually used in clinical devices, and carcinogenicity data are not available for a number of alloys which are commonly

used, including nickel–titanium.

Metal alloys containing a preponderance of *nickel* in combination with varying amounts of chromium, iron, gallium, copper, aluminium and manganese have been tested as powder or pellets by subcutaneous or intraperitoneal administration to rats and by intratracheal administration to hamsters. In these studies, local sarcomas were consistently found at the injection site in the treated animals and were absent in vehicle controls. One of the nickel-based alloys (which contained approximately 66–67% nickel, 13–16% chromium and 7% iron) was tested independently by two laboratories, using different species (hamsters and rats) and different routes of administration (intratracheal and intraperitoneal). In both studies, local tumours were seen in proportion to the dose of alloy. Local tumours were also observed in two bioassays in which rats received identification ear tags made of an alloy that contained 67% nickel, 30% copper, 2% iron and 1% manganese.

Most other nickel-containing alloys tested as powder and rods in rats by intramuscular, intraperitoneal, intrarenal and intraosseous administration gave negative or equivocal results for induction of tumours at the injection site. One study in hamsters by intratracheal administration of an alloy powder containing approximately 27% nickel, 39% iron and 16% chromium also gave negative results.

One clinically relevant alloy, Ni₃₅Co₃₅Cr₂₀Mo₁₀ (MP35N alloy), gave negative results for carcinogenicity when tested in two studies by intramuscular implantation in rats as rods, but produced local sarcomas in one study following intramuscular administration to rats as a powder.

Titanium-based alloys were tested in rats by intramuscular administration of rods and by intraosseous administration of rods and intra-articular administration of wear-debris. No local tumours were observed at the injection site in these experiments, except in one study by intraosseous administration in which a titanium/aluminium/vanadium alloy implanted into the femur as hemi-cylinders produced a high incidence of local tumours, especially where there was loosening of the implant.

Cobalt-based alloys were tested in rats by intramuscular administration. Local tumours were induced by a powder (particle size, 0.1–1 µm) in horse serum but not by dry powders (particle size, 0.5–50 and 100–250 µm) or by polished rods. No local tumours were observed in guinea-pigs following intramuscular injection of cobalt as a dry powder (particle size, 0.5–50 µm). A low incidence of local tumours was observed in rats following intraosseous administration of two cobalt-based alloys given as powder or wire. Local tumours did not occur following intraosseous implantation of rods of two other cobalt-containing alloys. No local tumours occurred in rats following intra-articular administration of a cobalt alloy powder.

Stainless steels containing 13–17% chromium were tested by intratracheal administration of powder to hamsters, intrabronchial administration of wire to rats and by intramuscular administration of rods and discs to rats and intraosseous administration of rods and powder to rats. No local tumours were observed, except in rats receiving stainless steel discs.

Thin foils of silver, gold, platinum, tin, steel, Vitallium (CoCrMo alloy) and tantalum were tested by subcutaneous implantation in rats. All of these foils produced local sarcomas.

In one study in rats, subcutaneous implantation of discs of aluminium oxide ceramic produced local sarcomas. In a few studies in mice and rats, local sarcomas were observed following subcutaneous implantation of glass sheets.

Numerous polymeric materials have been tested for carcinogenicity in mice and rats, most frequently by

subcutaneous, intramuscular or intraperitoneal injection. Many materials—cellophane, ϵ -caprolactone-L-lactide copolymer, polyamide (Nylon), poly(ethylene terephthalate), polyethylene, poly-L-lactide, poly(2-hydroxyethylmethacrylate), poly(methyl methacrylate), polypropylene, polystyrene, polytetrafluoroethylene, polyurethane, poly(vinyl alcohol), poly(vinyl chloride), polymethylsiloxane (silicone) film or polysilicone gum and vinyl chloride–vinyl acetate copolymers—produced sarcomas at the site of implantation with varying incidence. When several polymers were tested in rats according to the same experimental protocol, sarcoma incidences ranged from 70% (polypropylene) to 7% (silicone). A low incidence of local tumours was seen with silicone in five separate experiments using rats.

A few experiments with various polymeric materials have been reported using small number of other animal species, such as rabbits, guinea-pigs and hamsters, with generally negative findings.

Polymeric materials with a large surface area and a flat and smooth surface morphology generally induced a significantly increased incidence of sarcomas at the site of implantation. In most studies, perforated or foam materials or textiles induced lower incidences of sarcomas in comparison with flat films. Some studies suggest that surface roughening decreases local sarcoma incidence. The diameter and number of transmembrane channels (pores) per unit surface area are critical for this trend of decrease in sarcoma incidence. Segmenting or pulverizing polymeric materials significantly decreases local sarcoma incidences, often to nil.

For biodegradable polymers, the degradation rate is critical for local tumour induction in rodents. No local tumours were observed with poly(glycolic acid), which is quickly degraded within two months, whereas local sarcomas were induced by poly-L-lactide and ϵ -caprolactone-L-lactide copolymer which degraded more slowly (the polylactide degraded but was dimensionally unchanged at 24 months; ϵ -caprolactone-L-lactide copolymer fragmented after six months).

6.5 Other relevant data

The mutagenicity and carcinogenicity of a biomaterial are influenced by the exact composition of the biomaterial or extract(s); the composition and rates of release of leachable materials into the biological environment; degradation, which may lead to the formation of compounds with different mutagenic properties or leachability; the physical environment; and the surface properties. Much of the information available for assessment is inadequate in these respects, and methods are often not validated.

Wear and corrosion of metal implants result in the generation and release of a wide range of degradation products. The composition of the material surface or particles can vary as individual components are selectively removed or chemically modified. In the case of alloys, the release of one type of metal ion can be strongly influenced by the identity of other metals in the alloy. Most studies provide inadequate characterization data, but there is potential for the release of chemical species of known mutagenicity or carcinogenicity.

Experimental studies have shown that the potential for lead toxicity as a complication of lead projectile or bullet injury appears to be related to the surface area of the bullet (the greater the surface area, the greater the absorption), the location of the bullet (muscle or joint tissues), the presence of synovial fluid and length of time that the bullet resided in the body.

Available studies are inadequate to permit reliable and accurate estimates of long-term effects of depleted uranium in humans. Because of the low specific radioactivity of depleted uranium, the long-term toxicity is thought to be due to chemical rather than radiation effects.

Inflammatory (fibrotic) reactions have been observed with several non-metallic implant materials, including silicones and polyurethanes. Depending on the physical properties of the biomaterial, its presence can be associated with implantation-site sarcomas in rodents. There are insufficient data to conclude that a genotoxic mechanism operates in solid-state carcinogenesis. There are in-vitro data demonstrating the inhibitory effects of polyurethane, polyethylene and poly(ethylene terephthalate) on gap junctional intercellular communication.

Mutagenic properties of some biomaterial extracts have been demonstrated in some studies. The compounds shown or suspected to be responsible for this are components of the biomaterial, unreacted monomers or products of secondary reactions.

Data on the local and systemic availability of chemical species have been reported for only a limited number of biomaterials. In the case of poly(ester urethane) foam, biodegradation results in the generation of 2,4-diaminotoluene. This compound induces hepatocellular carcinomas when fed to mice and rats. There is no evidence that chemical carcinogenesis due to this compound plays a direct role in the mechanism of implant-site sarcoma development. There is no convincing evidence for the biodegradation of polydimethylsiloxanes (silicones).

Cytotoxicity of freshly cured dental composite materials and bonding agents has been demonstrated. Also, the components of resin composites all cause significant toxicity in direct contact with fibroblasts. However, the hazard for the dental pulp depends on the quantities which permeate the dentin and accumulate in the pulp.

A limited number of animal studies have shown pulpal responses to acid etching and bonding agents, which indicates a possible risk of pulpal reactions in patients. Composite materials may give rise to biological effects, but microleakage and bacterial infection complicate the evaluation of pulpal effects of composites.

Clinical reports on the adverse effects of composite filling materials indicate that pulpal and mucosal reactions rarely occur.

With few exceptions, the amounts of individual chemicals to which professionals and patients are exposed from adhesive agents and composite dental filling materials seem to be insufficient to cause clear, systemic toxic effects. Some constituents of adhesive agents and composite materials may have genotoxic potential. For most compounds of dental composites, there is little information on toxicity. With the exception of methyl methacrylate, no relevant data are available to compare local concentrations of released compounds with levels that produce toxic effects.

Formaldehyde has been shown to be released from some dental polymers *in vitro*, but the levels appear to be low.

6.6 Evaluation

There is *evidence suggesting lack of carcinogenicity* in humans of breast implants, made of silicone, for female breast carcinoma.

There is *inadequate evidence* in humans for the carcinogenicity of implanted prostheses made of silicone for neoplasms other than female breast carcinoma.

There is *inadequate evidence* in humans for the carcinogenicity of non-metallic implants other than

those made of silicone.

There is *inadequate evidence* in humans for the carcinogenicity of metallic implants and metallic foreign bodies.

There is *inadequate evidence* in humans for the carcinogenicity of orthopaedic implants of complex composition and of cardiac pacemakers.

No epidemiological data relevant to the carcinogenicity of ceramic implants or dental alloys of precious metals were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of implants of metallic cobalt, metallic nickel and for nickel alloy powder containing approximately 66–67% nickel, 13–16% chromium and 7% iron.

There is *limited evidence* in experimental animals for the carcinogenicity of implants of alloys containing cobalt and alloys containing nickel, other than the specific aforementioned alloy.

There is *inadequate evidence* in experimental animals for the carcinogenicity of implants of chromium metal, stainless steel, titanium metal, titanium-based alloys and depleted uranium.

There is *sufficient evidence* in experimental animals for the carcinogenicity of polymeric and metallic materials in the form of thin films, foils or sheets when implanted into connective tissues of rodents.

There is *inadequate evidence* in experimental animals for the carcinogenicity of poly(glycolic acid) implants.

There is *inadequate evidence* in experimental animals for the carcinogenicity of polymeric materials in the form of powders when inserted into connective tissues of rodents.

There is *inadequate evidence* in dogs for the carcinogenicity of metallic implants and metallic and non-metallic foreign bodies.

There is *limited evidence* in cats for the carcinogenicity of certain feline vaccines containing adjuvants.

Overall evaluation

Organic polymeric materials as a group are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Polymeric implants prepared as thin smooth films (with the exception of poly(glycolic acid)) are *possibly carcinogenic to humans (Group 2B)*.

Orthopaedic implants of complex composition and cardiac pacemakers are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Silicone breast implants are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Metallic implants prepared as thin smooth films are *possibly carcinogenic to humans (Group 2B)*.

Implanted foreign bodies of metallic cobalt, metallic nickel and an alloy powder containing 66–67% nickel, 13–16% chromium and 7% iron are *possibly carcinogenic to humans (Group 2B)*.

Implanted foreign bodies of metallic chromium or titanium and of cobalt-based, chromium-based and titanium-based alloys, stainless steel and depleted uranium are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Dental materials are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Ceramic implants are *not classifiable as to their carcinogenicity to humans (Group 3)*.

For definition of the italicized terms, see Preamble Evaluation.

Last updated: 23 November 1999

Pathologie traditioneller chirurgischer Netze zur Hernienreparation nach Langzeitimplantation im Menschen

B. Klosterhalfen^{1,2,3}, U. Klinge^{3,4}, B. Hermanns¹ und V. Schumpelick⁴

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Pathology of traditional surgical nets for hernia repair after long-term implantation in humans

Summary. The widespread use of alloplastic materials as the standard procedure for hernia repair makes an evaluation of the long-term integration of these implants imperative. A total of 121 explanted meshes (mean implantation time 23.2 ± 19.7 months) of polypropylene (Atrium®, n = 20; Marlex®, n = 50; Prolene®, n = 21), Polyester (Mersilene®, n = 19) and PTFE (Gore-Tex®, n = 11) were analyzed in regard to the tissue and cell response within the interface mesh-fiber/tissue. The mesh samples were investigated by light and electronmicroscopy, as well as immunohistochemistry. The morphometric results confirmed a persisting inflammatory proliferative foreign-body reaction with increased cell turnover in the recipient tissues. This reaction is mainly influenced by the selected mesh modification. The consequences of the arising "chronic wound" are discussed in detail, in particular with regard to possible malignant transformation.

Key words: Hernia - Surgical mesh, pathological risk-analysis.

wird. Die möglichen Folgen dieser „chronischen Wunde“ insbesondere im Hinblick auf eine mögliche Fremdkörper-induzierte Carcinogenese werden kritisch diskutiert.

Schlüsselwörter: Hernie - Chirurgische Netze, pathologische Risikoanalyse.



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B. Klosterhalfen et al.: Pathologie traditioneller chirurgischer Netze zur Hernienreparation nach Langzeitimplantation im Menschen 51

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Conceptus.

V1

October 15, 2002

(b) (6)
Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: Amendment to PMA No. P020014
Partial Response to Approvable Letter (Item #2)
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

We are in receipt of the Agency's letter of September 30, 2002, stating that the PMA application for the Essure System is approvable (P020014). This PMA Amendment is to respond to item #2 in the approvable letter. Specifically, item #2 requested "complete safety and effectiveness data from the pivotal clinical study, including the last two study subjects scheduled for their 12-month visit late this month;". The other items in the approvable letter will be formally responded to after we receive final feedback from the Agency regarding our submitted draft versions of the labeling, training manual and post-approval study protocols.

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2002 OCT 19 AM 11
FDA/CDRH/OCE/PMO

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PMA Amendment, P020014
Partial Response to Approvable Letter
Updated Phase II and Pivotal Trial Study Reports

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PMA Amendment, P020014
Partial Response to Approvable Letter
Updated Phase II and Pivotal Trial Study Reports

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Sincerely,

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Enclosures: Volumes 1-10

PMA Amendment, P020014
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Conceptus Essure™ System

Amendment to PMA No. P020014

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Amendment to PMA No. P020014
Final Phase II Study and Pivotal Trial Reports
October 15, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

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Exhibit F -- Study Deviations

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REFER TO VOLUME 3 OF APRIL 19, 2002 PMA FOR THE BELOW
DOCUMENTS**

- Exhibit A - Study Protocol
- Exhibit B - Informed Consent Form
- Exhibit C - Statistical Plan (Final Clean Copy)
- Exhibit D - Statistical Plan (with Changes Noted)

**Volume 4 –NOT RECOPIED FOR THIS AMENDMENT. PLEASE
REFER TO VOLUME 4 OF APRIL 19, 2002 PMA FOR THE BELOW
DOCUMENTS**

- Exhibit A - Patient Questionnaires
- Exhibit B - Electronic Case Report Forms

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Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

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Amendment to PMA No. P020014
Final Phase II Study and Pivotal Trial Reports
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Summary Data Tables:

Months of Wearing and Effectiveness

6 Month PAC Visit

12 Month PAC Visit

18 Month PAC Visit

24 Month PAC Visit

Adverse Events up to 1 Year

Adverse Events up to 2 Years

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*This patient completed her one-year follow-up visit after the above Summary Data Tables were already printed. Therefore, a copy of her Case Report Form is included as an addendum to the Summary Data Tables.

Volume 11-

**NOT RECOPIED FOR THIS AMENDMENT. PLEASE REFER TO
VOLUME 11 OF JUNE 5, 2002 PMA AMENDMENT FOR THE
BELOW DOCUMENTS**

References for Pivotal Trial Report

II. Clinical Data: Phase II Study

A. Background

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The data in this report are as of October 8, 2002.

¹ FDA's letter is actually date-stamped January 19, 1998 in error.

Figure II.1: Clinical Development Pathway(b)(4)
**B. Study Purpose and Protocol**

This study was a prospective, multi-center, international study of women seeking permanent contraception. Investigational sites were located in the United States, Belgium, Spain, and Australia. All sites conducted the study according to virtually the same protocol as that approved under the IDE (see **Exhibit B**), and obtained approval from an Institutional Review Board (IRB) or Ethics Committee (EC) before study commencement. A protocol revision history is provided in **Exhibit C**.

All sites were monitored according to the same standard operating procedures (SOPs) in accordance with the U.S. Good Clinical Practice (GCP) medical device regulations, informed consent provisions of the Declaration of Helsinki, and the European Standard EN540: Clinical Investigations of Medical Devices for Human Subjects.

The objectives of this study were to evaluate:

- The woman's tolerance of, and recovery from, the Micro-insert placement procedure;
- The safety of the Micro-insert placement procedure;
- The woman's tolerance of the implanted Micro-inserts;

- The long-term safety and stability of the implanted Micro-inserts; and
- The effectiveness of the Micro-inserts in preventing pregnancy.

Screening

Women who read and signed the Informed Consent Form were interviewed for demographic and socioeconomic data. They then underwent a pelvic exam and were screened for *Neisseria gonorrhoea* and *Chlamydia trachomatis* infections, hemoglobin and white blood cell count. Women also had a Pap Smear performed (unless there was a record of a normal Pap Smear within the previous 12 months).

Placement procedure

The placement procedure was performed as described in the attached protocol. During the study there were two changes to the Essure System that affected the Micro-insert placement procedure. A black marker bump was added to the Delivery Catheter to aid in initial positioning (this change was submitted in a 5-day Notification dated October 7, 1999) and a one-handed release mechanism (handle) was added to improve ergonomics of Micro-insert placement (this change was submitted in a 5-Day notification dated March 6, 2000). Other minor changes to the Micro-insert and/or Delivery System were noted in an annual IDE progress report dated October 20, 1999. A detailed description of the design history for the Gamma design was provided in Module I, Device Description, Attachment 2.

Follow-up procedures

All women filled out a questionnaire one week after Micro-insert placement, documenting any bleeding, discomfort or other symptoms they experienced following the procedure. They were also asked about their perceptions of the placement procedure. Women then kept diaries for 6

months detailing menstrual and sexual activity, as well as accompanying symptoms.

During the first three months following Micro-insert placement, women were required to use an alternative form of contraception. This alternative contraception period was to allow adequate time for the tissue in-growth process to occlude the fallopian tube. Women could choose a barrier method or oral contraceptives for their alternative contraception.

At three months post-procedure, women underwent a hysterosalpingogram (HSG) and an ultrasound (USG) or an HSG alone to determine Micro-insert position and retention, and to evaluate occlusion of the fallopian tubes. If the Micro-inserts were in a satisfactory location, women were advised to discontinue alternative contraception and rely on the Micro-inserts for contraception. Women were then followed at the 6, 12, and 18-month post-procedure time points, and 24 and 36-months after discontinuation of alternative contraception^{2,3}. Information was collected on case report forms (**Exhibit E**) and submitted for data entry and data report preparation by an independent firm, (b)(4)

C. Inclusion and Exclusion Criteria

Study participants were women who were seeking permanent contraception.

The objectives of the inclusion and exclusion criteria were to:

- Ensure prior fertility

² In earlier versions of the protocol, women were followed up at 4 and 5 months with an USG. In addition, these women underwent assessment of Micro-insert position via ultrasound at the 6, 12 and 24-month visit.

³ The protocol was changed in March 2001 to move the 24-month post-procedure visit to 24 months of relying on the Essure Micro-insert (27 months post-procedure) in order to align the Phase II protocol with the Pivotal trial protocol for follow-up visits. Two women completed the 24-month visit as originally scheduled at 24 months post-placement, however, and a phone call three months later confirmed the responses given at their earlier visit.

- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

The detailed inclusion and exclusion criteria are provided in the protocol, **Exhibit B.**

D. Number of Investigators/ Subjects per Investigator

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Table II.1: Distribution of Investigators/ Number of Women Undergoing Placement

Investigator	Number of Women
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E. Study Population/Study Period

Study participants were women seeking permanent contraception. Permanent contraception candidates were screened for eligibility to participate in this clinical study. Candidates who met the inclusion and exclusion criteria and who were willing to participate in the study were provided with an Informed Consent for their review and signature prior to screening tests. The Investigator or his/her designee fully informed the woman of the potential risks and benefits of study participation, according to the Informed Consent approved by the overseeing Institutional Review Board/Ethics Committee. A copy of the Informed Consent is attached as **Exhibit D⁴**. The woman was given the opportunity to discuss any

⁴ Modifications to the standard consent form were made at some sites in order to address changes or formatting requested by the reviewing IRB/EC. Copies of site-specific consent forms can be supplied if requested.

questions she might have and was instructed that she could decline participation at any time prior to the performance of the procedure.

The study commenced (with the Gamma design) in November 1998⁵ and enrollment ended in June 2000, at which time 269 women had been enrolled in the study (signed the informed consent and underwent the screening process). 227 women underwent a Micro-insert placement procedure. The remaining 42 women voluntarily withdrew from the study, were excluded at the time of screening or were enrolled into the Pivotal Trial instead. See **Diagram II.1** for a Patient Accountability Tree.

⁵ The study commenced in Australia in November 1998, but the IDE sites did not enroll patients until after conditional IDE approval in January 1999.

F. Patient Tree
Diagram 1. Patient Accountability Tree

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G. Study Demographics

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H. Micro-insert Placement Rate

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October 15, 2002

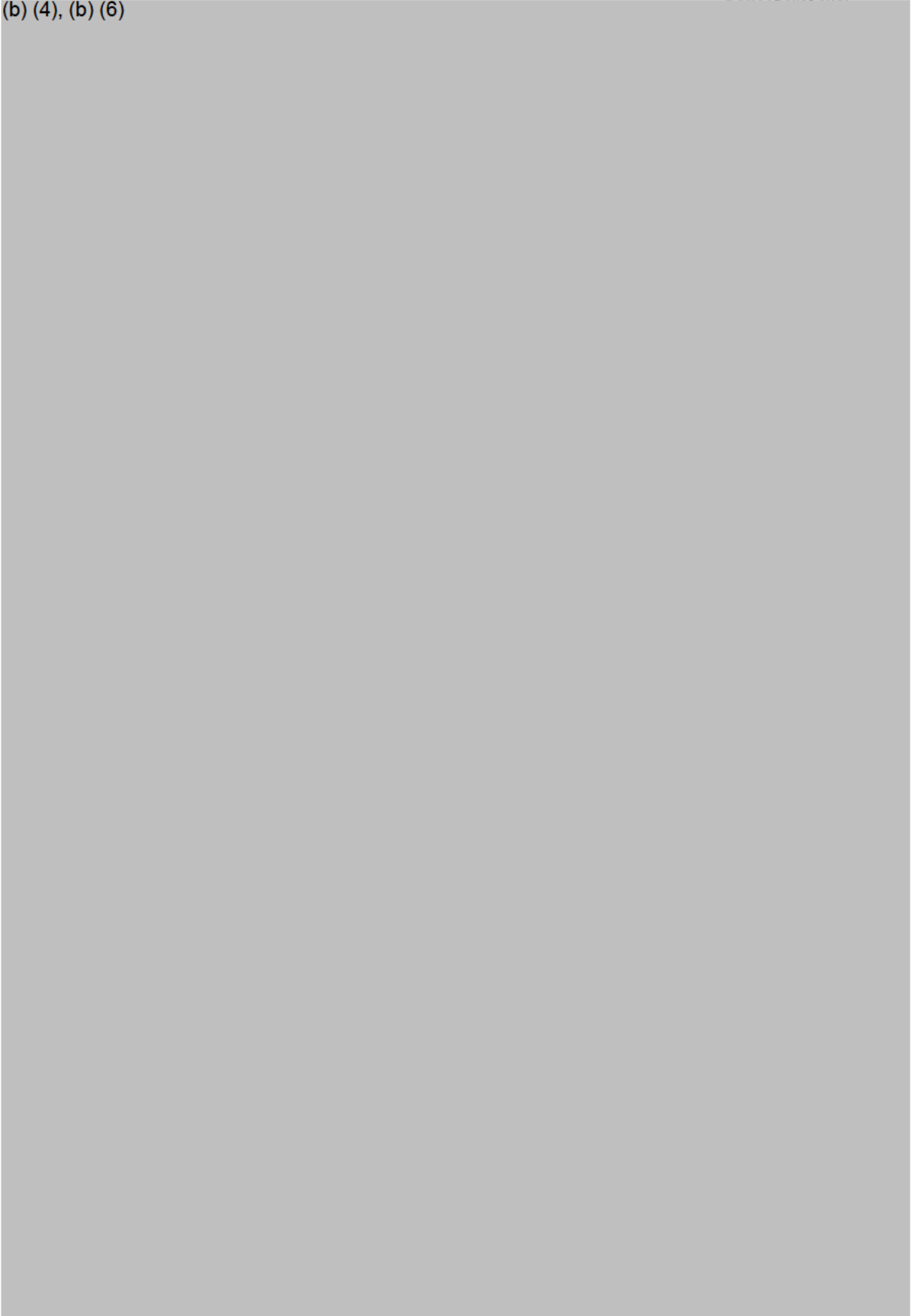
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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov


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One-week Questionnaire

(b) (4)



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HSG Results

(b) (4)



Beta study group). The HSG findings are provided in **Figure II.2 and Table II.14.**

Figure II.2. HSG Findings

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Retrospective Analysis of HSGs

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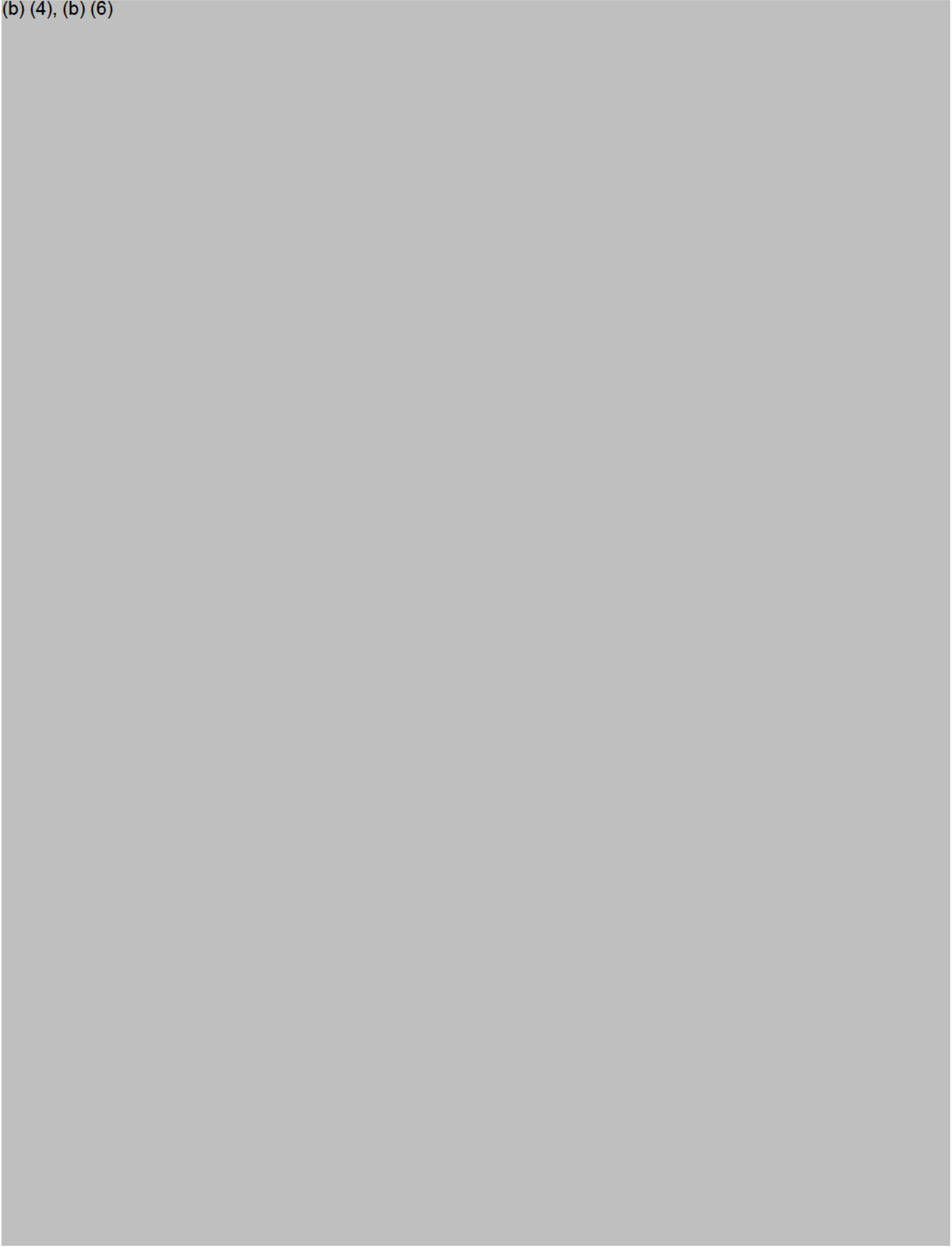
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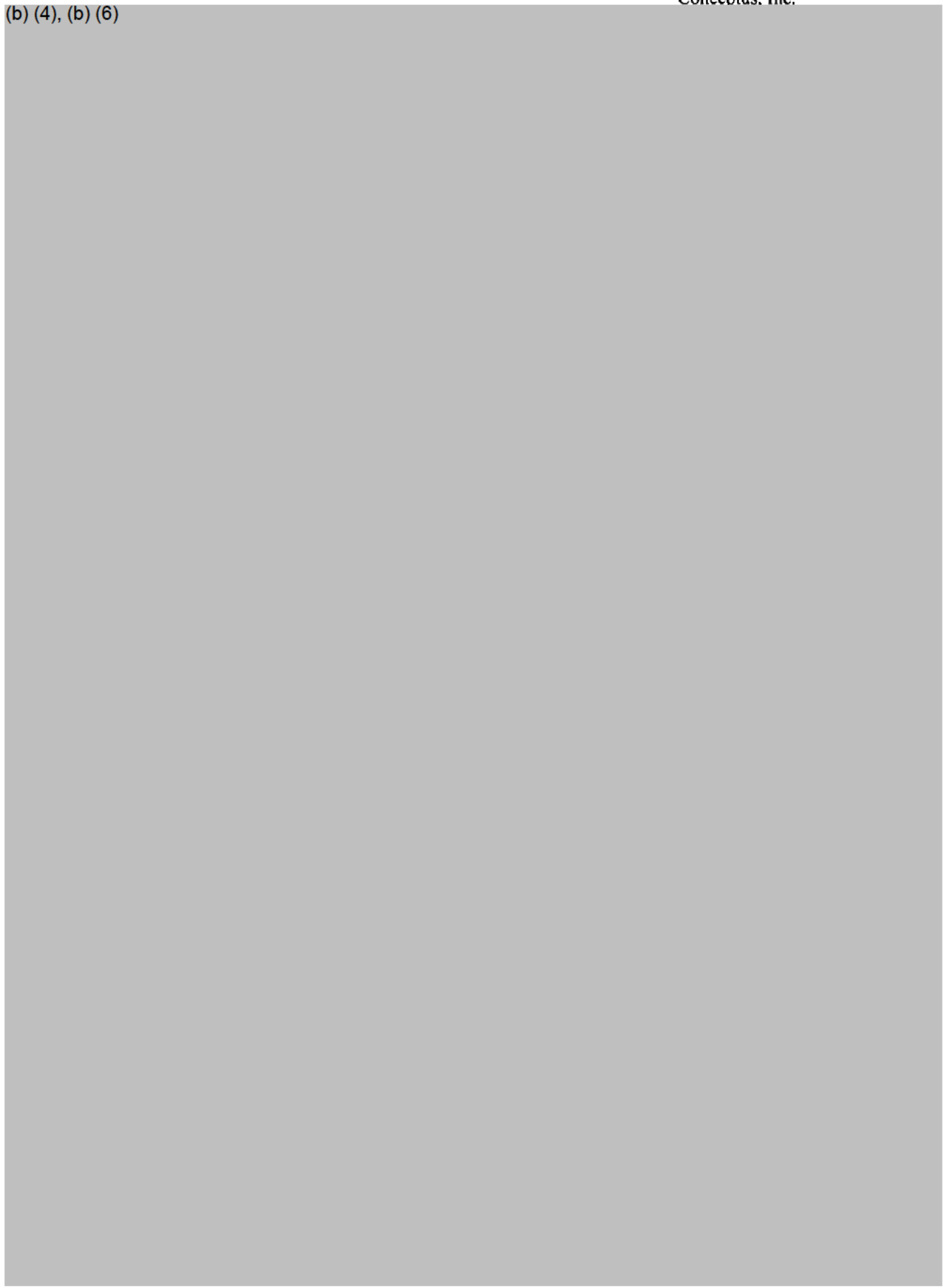
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40

(b) (4)



48

K. Effectiveness

(b) (4)



(b)(4)



L. Justification for Use of Foreign Data

The protocol used by all study sites had the same study endpoints and relied upon the same set of study visits to determine the outcome of the endpoints. All protocols were reviewed and approved by a local overseeing Ethics Committee or IRB. All procedures were performed using a standard hysteroscopic approach under the preferred anesthesia regimen of the Investigator. There were no major differences in

hysteroscopic equipment used or anesthesia regimen between Investigators from different countries.

M. GCP Compliance Statement

The study was conducted in accordance with US Good Clinical Practice (GCP) Regulations (21 CFR 812, 50, and 56).

N. Case Report Forms/Data Tabulations

Relevant data was recorded on standardized case report forms, a sample of which is attached as **Exhibit E**. The data were summarized in tabular format, with means, standard deviations and sample size. Data tables are included in **Exhibit G**.

Completed case report forms are kept in the Investigators' facilities. Forms at all sites are accessible to the Investigator, his or her authorized staff, and representatives of Conceptus, Inc. for the purpose of monitoring the study and auditing the data and patient records.

O. Study Deviations

Deviations to the study protocol are included in **Exhibit F**.

P. Device Accountability

Conceptus personnel carried all devices to the investigational sites. Devices were accounted for on device accountability logs and all unused and damaged devices were returned to Conceptus by company personnel. In addition, all delivery system parts were returned to Conceptus for evaluation. No product was left at an investigational site.

Q. Conclusions Drawn From the Study

44

The Essure Micro-insert placement procedure was found to be safe and acceptable to women. The procedure-related adverse events were within an expected and acceptable range for a hysteroscopic procedure, with less than 1% of women experiencing an adverse event on the day of the procedure. Adverse events experienced after the day of the procedure that prevented reliance on Essure occurred in less than 4% of women.

The primary adverse event experienced was perforation. Of the perforations, 4/6 (67%) utilized the Support Catheter, which was associated with a high rate of perforation. The Support Catheter was discontinued prior to commencement of the Pivotal Trial, and the perforation rate in the Pivotal Trial was less than 1%.

The long-term acceptability of wearing the Essure Micro-inserts was found to be "good" to "excellent" in 99% of women who have been followed for 1-3 years.

The observed one-year effectiveness rate of 100% (98.47%-100%) and the two-year effectiveness rate of 100% (98.45%-100%) are comparable to other methods of sterilization currently available¹².

Thus, although the Phase II trial was initially designed to serve as a preliminary study of safety and effectiveness for purposes of supporting commencement of a Pivotal Trial, the data from this study support the safety, effectiveness, and patient satisfaction with the Essure placement procedure and the implanted Micro-insert.

¹² FDA Guideline: "Guidance for Industry, Uniform Contraceptive Labeling", dated July 23, 1998.

**EXHIBIT A: SUMMARY OF RESULTS WITH BETA DESIGNS OF
THE STOP DEVICE**

46

Summary of results with Beta designs of the STOP device

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Figure 1.

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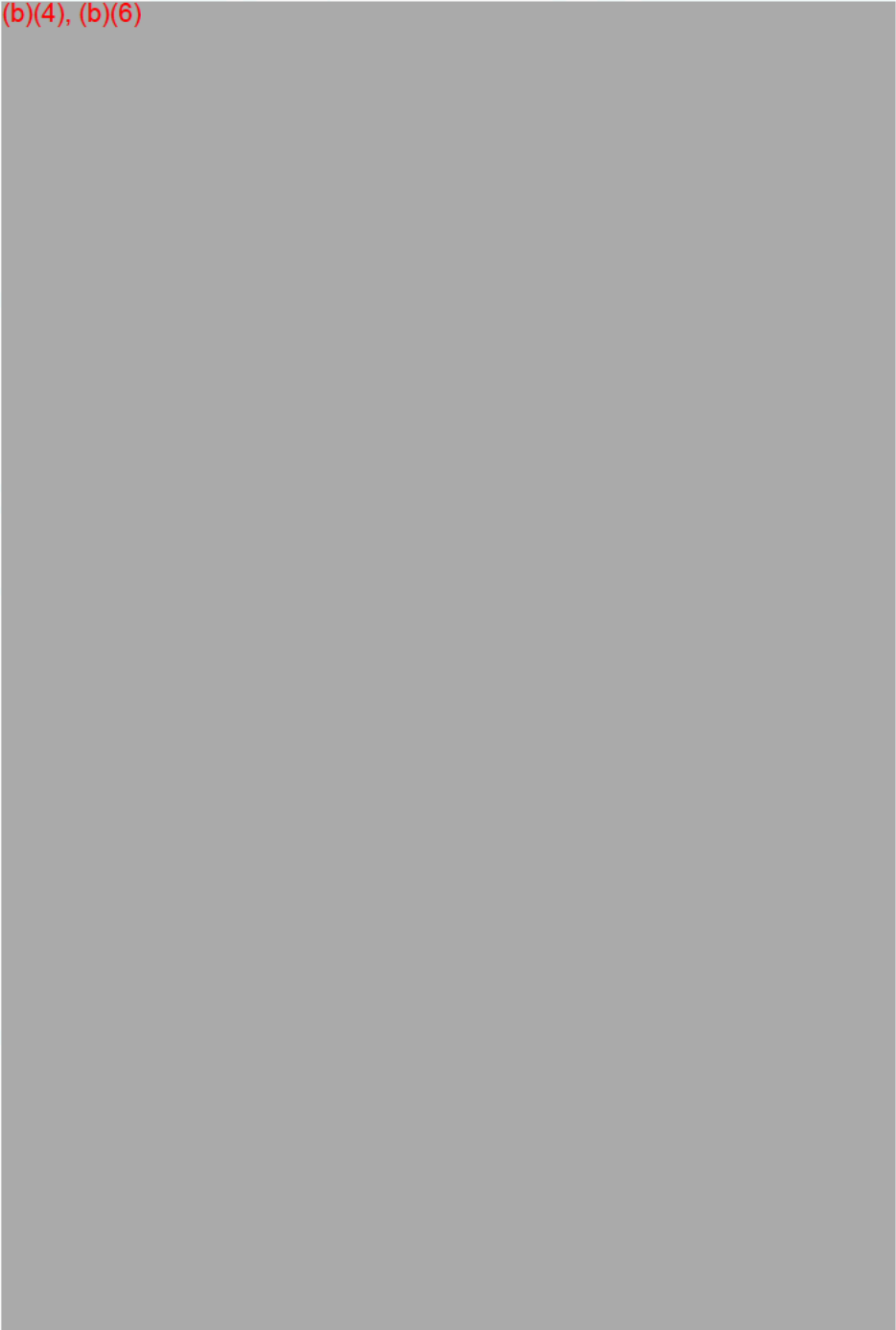


EXHIBIT B: PROTOCOL APPROVED UNDER THE IDE

A Multi-Center Clinical Trial To Evaluate the Safety and Effectiveness of the STOP Device To Prevent Pregnancy in Women Who Are Seeking Permanent Contraception

Conceptus Protocol #: STOP 10

Research Protocol

**Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070**

(b) (6)

REVISION HISTORY

Original Protocol, Rev 00

06/19/98

Protocol, Rev 01

03/16/99

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1. TITLE

“A Multi Center Clinical Trial To Evaluate the Safety and Effectiveness of the STOP Device To Prevent Pregnancy in Women Who Are Seeking Permanent Contraception.”

2. PURPOSE OF STUDY

The purpose of this study is to evaluate the ability of the STOP device to safely and effectively prevent pregnancy in women who are seeking permanent contraception.

3. INVESTIGATORS AND QUALIFICATIONS

The Investigator selected to participate in this study is (b) (6) is a gynecologist who has participated in both the peri-hysterectomy and pre-hysterectomy studies of the STOP device. He has extensive experience in hysteroscopy, with an adequate participant population and clinical research staff to support the study objectives and timelines.

4. PARTICIPANTS

Study participants will be women who are seeking permanent contraception. Prior to taking part in the study, the Investigator or his or her designee will fully inform the participant of the potential risks and benefits of study participation, according to the Information Sheet and Informed Consent approved by the overseeing Ethics Committee and Section 9 of this protocol. The participant will be given the opportunity to discuss fully any questions she may have.

5. INCLUSION AND EXCLUSION CRITERIA

The study population will consist of 10 participants in whom bilateral device placement is achieved. The participants may be transferred into other studies evaluating long term safety and efficacy, if they consent to such participation. It is expected that more than 10 participants may need to be enrolled in order to obtain 10 participants in whom bilateral placement is achieved. A maximum of 15 patients will be enrolled. The inclusion and exclusion criteria are listed below.

5.1 Inclusion Criteria

- 5.1.1 Women who are aged 25 to 42;
- 5.1.2 Women who are at risk for becoming pregnant;
- 5.1.3 Women who have at least one living child, who is at least 1 year old;
- 5.1.4 Women who are seeking permanent contraception;
- 5.1.5 Women who can accept the risk of pregnancy occurring while relying on the STOP device for prevention of pregnancy;
- 5.3.1 Women who agree to undergo STOP device placement under hysteroscopic control, in an office or ambulatory setting;
- 5.1.7 Women who are able and willing to use a barrier or oral method of contraception (<35 mcg of estrogen), for the first three months following STOP device placement;
- 5.1.8 Women who are willing to keep a coital/menstrual log for 6 months following the device placement procedure;
- 5.1.9 Women with regular, cyclical menses within 2 months prior to the device placement procedure;
- 5.1.10 Women who can be available for all study visits;
- 5.1.11 Women who are able to understand the risks and benefits of participating in the study and willing to provide written, informed consent.

5.2 Exclusion Criteria

- 5.2.1 Women who are unsure about their desire to end their fertility;
- 5.2.2 Women who, in the Investigator's medical opinion, are not suitable candidates for the STOP device placement procedure;

- 5.2.3 Women with an abnormal uterine cavity or fallopian tubes or structurally abnormal uterus or fallopian tubes that makes visualization of, or access to, the ostia difficult;
- 5.2.4 Women with cervical or uterine neoplasia or its precursors;
- 5.2.5 Women with untreated acute cervicitis;
- 5.2.6 Women with unexplained abnormal uterine bleeding or intermenstrual bleeding within three months prior to the device placement;
- 5.2.7 Women who have not had at least one normal period within 3 months after the following gynecological events: irregular periods treated with oral contraceptives which have since been discontinued, IUD removal, childbirth, or termination of pregnancy;
- 5.2.8 Women who have not had two regular menses since stopping the use of oral contraceptives, implants (including levonorgestrel- and desogestrel-containing implants) or Depo Provera;
- 5.2.9 Women with a history of chronic pelvic pain, severe dysmenorrhea, or severe dyspareunia;
- 5.2.10 Women who have had both fallopian tubes removed, ligated or have had surgery to repair the fallopian tubes;
- 5.2.11 Women with unresolved tubal, ovarian or endometrial pathology;
- 5.2.12 Women diagnosed with postpartum endometritis or infection from an abortion in the last 3 months;
- 5.2.13 Women currently diagnosed with acute pelvic inflammatory disease or a history of pelvic inflammatory disease without subsequent pregnancy;
- 5.2.14 Women who are contraindicated for surgery; and

5.2.15 Women with a known allergy to contrast media.

5.3 Withdrawal Criteria:

5.3.1 Study participants may withdraw from the study at any time. The Investigator will discuss with the participant any medical follow up that may be required.

6. PLAN AND DESIGN

6.1 Purpose

The purpose of this study is to evaluate the ability of the STOP device to safely and effectively prevent pregnancy in women who are seeking permanent contraception.

6.2 Study Objectives

The objectives of this study are to evaluate:

- a) the participant's tolerance of and recovery from the device placement procedure;
- b) safety of the device placement procedure;
- c) the participant's tolerance of the implanted device;
- d) long-term safety and stability of the implanted devices; and
- e) the effectiveness of the device in preventing pregnancy.

6.3 Study Design

This is a multi-center, non-comparative clinical trial of the STOP device in approximately 10 participants in whom bilateral device placement is achieved. The STOP device will be placed in participants who are seeking permanent contraception.

It is estimated that the study enrollment will be completed in approximately 3 months from the date the study starts. Study participants will be followed for two years. Study participants may be transferred to other studies of the STOP device to evaluate long term safety and efficacy, if they consent to such participation.

6.4 Study Procedures

Study procedures are summarized in Appendix A, Schedule of Events.

6.4.1. Visit 1 Participant Screening

6.4.1.1 Eligibility

Permanent contraception candidates will be screened for eligibility to participate in this clinical study. Candidates who meet the eligibility criteria and who are willing to participate in the study will be provided with an Information Sheet and Informed Consent for their review and signature prior to study participation. Candidates will be given ample time to consider their decision to enroll in the study.

6.4.1.2 Screening

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6.4.2 Visit 2 - STOP Device Placement Procedure

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6.4.3 Summary of Steps for Device Placement

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7. ADVERSE DEVICE EFFECTS

Adverse events are defined as any untoward deviations in subject health away from baseline. Investigators must record and document all device related adverse effects in the case report form, and report any unanticipated device related adverse effects to Conceptus and the reviewing IRB as soon as possible but no longer than 5 working days after becoming aware of the event.

8. ANALYSIS AND REPORTING OF RESULTS

Relevant data will be recorded on case report forms. The data will be summarized in a tabular format, with means, standard deviations and sample size.

Sample case report forms will be provided, if requested.

Completed case report forms will be kept in the Investigator's facilities. Forms will be accessible to the Investigator, his or her authorized staff, and to representatives of Conceptus, Inc. for the purpose of monitoring the study and auditing the data and patient records. The United States Food and Drug Administration (FDA) or other health authority also may require access to the forms and patient records.

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9. ETHICAL CONSIDERATIONS

Eligible study candidates will be women who are seeking fallopian tubal permanent contraception. Candidates will be fully informed of the potential irreversibility of the study procedure, and the risks and potential benefits associated with the procedure. The participant should be allowed ample time between the giving of consent and undergoing the study procedure to consider her decision and to ask questions. Additionally, participants must be willing to accept the risk that pregnancy could occur while relying on the STOP device for prevention of pregnancy. To ensure understanding of the study risks and benefits, as well as the intended permanent nature of the device, the informed consent procedure will be carried out at the initial interview and confirmed, in writing, on the day of the device placement.

9.1 Risks

Following are the potential risks associated with the device and the device placement procedure.

9.1.1 There is a risk of pregnancy and ectopic pregnancy and treatment for both. If the participant chooses to continue an intrauterine pregnancy, she will be informed that the risks of the device to the participant, to the fetus and to the continuation of the pregnancy are unknown. The participant will be responsible for all costs associated with the pregnancy, delivery, and raising the child, including any complications that may be related to the STOP device. Conceptus will pay for all treatment related to an ectopic pregnancy. If the participant wishes to terminate the pregnancy, Conceptus will pay for all costs related to the termination.

9.1.2 Pain, cramping and vaginal bleeding have been reported in tubal catheterization procedures performed for diagnosis of proximal tubal occlusion. This risk is discussed here because of the similarities in the technique used for fallopian tube access and the fallopian tube segment that is accessed in both procedures. Use of hysteroscopic visualization

may allow the Investigator to reposition the hysteroscope away from the origin of the pain. Typically, these incidents are minor and the cramping is similar to that experienced with a normal period. Intravenous sedation, analgesia or local anesthesia may be administered to the participant to prevent or reduce the participant's discomfort. Intravenous sedation, analgesia or rapid intravascular absorption of local anesthesia may result in dizziness, or fainting, for which treatment is typically not required. The participant should be able to resume normal activities within several hours of the procedure.

9.1.3 Abdominal/pelvic pain and cramping may occur as long as the devices remain in place. The pain and cramping may be more likely to occur during menstrual periods and during and after sexual intercourse. This pain is expected to be minor and similar to that experienced with a normal menstrual period.

9.1.4 During any x-ray procedure there is exposure to radiation. Exposure to radiation will be kept to a minimum by performing the minimum number of x-rays required to evaluate fallopian tube occlusion and device location. As reported by Thurmond, the radiation dose required for catheterization of the fallopian tubes is equivalent to estimated ovarian doses for a barium or excretory urogram (Thurmond A. Selective Salpingography and Fallopian Tube Recanalization. AJR 1991; 156:33-38).

9.1.5 Perforation or dissection of the fallopian tube or uterine cornua has been reported in approximately 4% of cases involving catheterization of the fallopian tube for diagnosis of proximal tubal occlusion (PTO). This rate is quoted here because of the similarity in the technique for tubal access and the fallopian tube segment that is accessed. Bleeding and scarring may result from such a perforation or dissection; however, treatment is typically not required, and no permanent effects have been noted in the clinical literature or in unpublished animal and clinical trials of falloposcopy conducted by Conceptus.

9.1.6 There is a risk of uterine perforation by the hysteroscope, which could result in possible injury to the bowel, bladder, and major blood

vessels. Surgical intervention would likely be required if such injury were to occur. The risk of uterine perforation associated with this procedure is low because manipulation of the hysteroscope is limited to that required to insert the hysteroscope through the cervix, into the uterus, and to visualize the fallopian tubal ostium. The uterine fundus and walls can be hysteroscopically visualized during manipulation and advancement of the hysteroscope, which will reduce the risk of perforation. To further reduce the risk of uterine perforation, the procedure will be terminated if excessive force is required to achieve cervical dilatation.

9.1.7 There is a risk of fluid absorption due to the saline fluid which will be used for distention of the uterus to place the hysteroscope; however, this is expected to be a remote risk due to: 1) the short time necessary for the device placement procedure; and 2) no resection, laceration or other disturbance of the endometrium is intended. If excess fluid absorption occurs, the body should eliminate the fluid through sweat and urine.

9.1.8 As with currently available methods of permanent contraception, if the device is to be removed, surgery may be required. Further, it is possible that surgical removal of the fallopian tubes and uterus may be required.

9.1.9 The emotional side effect for most women who have a permanent contraception procedure is a feeling of freedom from the fear of pregnancy. Sometimes, a woman is mildly depressed for a short time; this is normal. Occasionally, a woman may regret her decision to undergo permanent contraception.

9.1.10 There is a risk that the STOP device could move out of the fallopian tubes. Additional x-rays or ultrasounds may be required to identify the location of the devices, and surgery may be required to remove the devices.

9.1.11 As with all invasive procedures, the device placement procedure can cause an infection. An infection could cause damage to the uterus, fallopian tubes, or pelvic cavity. This could require antibiotic therapy, hospitalization, or surgery, including hysterectomy.

9.1.12 The use of contrast media, used to perform the HSG, has been associated with allergic reaction in some patients undergoing cardiovascular radiological procedures. Allergic reaction can result in hives or difficulty breathing. In some individuals, an anaphylactic response may occur which can lead to death.

9.1.13 As with any experimental device, there is the potential that unknown risks exist.

If the participant experiences a complication, her progress will be followed until it has resolved or is not expected to change.

9.2 Precautions

Any intrauterine procedure such as dilatation and curettage (D&C) or endometrial ablation or resection could interrupt the ability of the devices to prevent pregnancy.

9.3 Potential Benefits

There is a possible benefit to the participant if the STOP device is found to be safe and effective in preventing pregnancy. Since the STOP device is placed using a non-incisional technique, it is possible that the STOP device placement procedure may be less painful, less risky, less costly, or require a shorter period of recovery than surgical methods that are currently used. Also, the STOP device procedure will not leave an abdominal scar.

10. OTHER ETHICS COMMITTEE APPROVAL

A protocol with a similar study plan was submitted to the Ethics of Human Research Committee of the North Western Adelaide Health Service in Australia, and was approved on 30 April, 1997.

11. DATE OF COMMENCEMENT

The proposed date of commencement is July, 1998. It is estimated that the study enrollment at the site will be completed in approximately 3 months from the date the study starts. Study participants will be followed for two years.

12. MANUFACTURING

All STOP devices will be manufactured at Conceptus, Inc., in San Carlos, California, USA, according to Good Manufacturing Practices. Manufacturing steps are briefly described in Section V of the IDE.

13. INVESTIGATOR'S SIGNATURE

The Investigator will be required to sign the following statement, after reviewing the protocol.

I have carefully read and I understand the provisions of this protocol, and I agree to follow it in every detail. Furthermore, I understand that any changes to the protocol must be pre-approved by Conceptus, Inc. and the reviewing Ethics Committee or Institutional Review Board. I agree not to release to any third party, either during or after the study, any information about the STOP device, or about the study. All data for this study will be provided to Conceptus, Inc. and remains the sole property of Conceptus. I agree that any presentation or publication of study data will be pre-approved by Conceptus, Inc. I affirm that the base data used in the research will be stored safely and kept confidential, and will only be used for the purpose for which it has been approved.

INVESTIGATOR'S SIGNATURE DATE

Appendix A: Schedule of Events

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STOP 10 Protocol
IRB Approved: March 16, 1999

CONFIDENTIAL

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

**Appendix B: Protocol for Managing Participants Who Have Experienced Device
Expulsion or Migration**

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EXHIBIT C: PHASE II PROTOCOL REVISION HISTORY

PHASE II PROTOCOL REVISION HISTORY¹³

The Phase II protocol was revised twice during the course of the study: September 1999 and March 2001. The September 1999 revision was not made at all sites, however, because at that time study enrollment was thought to be complete at the sites where the amendment was not made. The March 2001 revision was made at all sites, and the revisions were made to align the Phase II protocol with the protocol for the Pivotal Trial. Each of the two protocol amendments is discussed separately below.

September 1999

The Phase II study, with the Gamma design, began in Australia in November 1998. An IDE supplement¹⁴ was filed in December of 1998, and conditionally approved in January of 1999 to begin the study at U.S. sites. In September 1999, the protocol was revised, but the protocol revision was not implemented at the US IDE sites (or at (b)(6) (b)(4)) because enrollment was thought to be near completion at those sites. **Tables 1 and 2** below depict the Schedule of Events for the sites (b)(4), (b)(6)

As can be seen, the main differences between the two Groups were: 1) the elimination of the 4 and 5 month visits, 2) the elimination of the use of ultrasound to evaluate device location and retention, 3) moving the pelvic

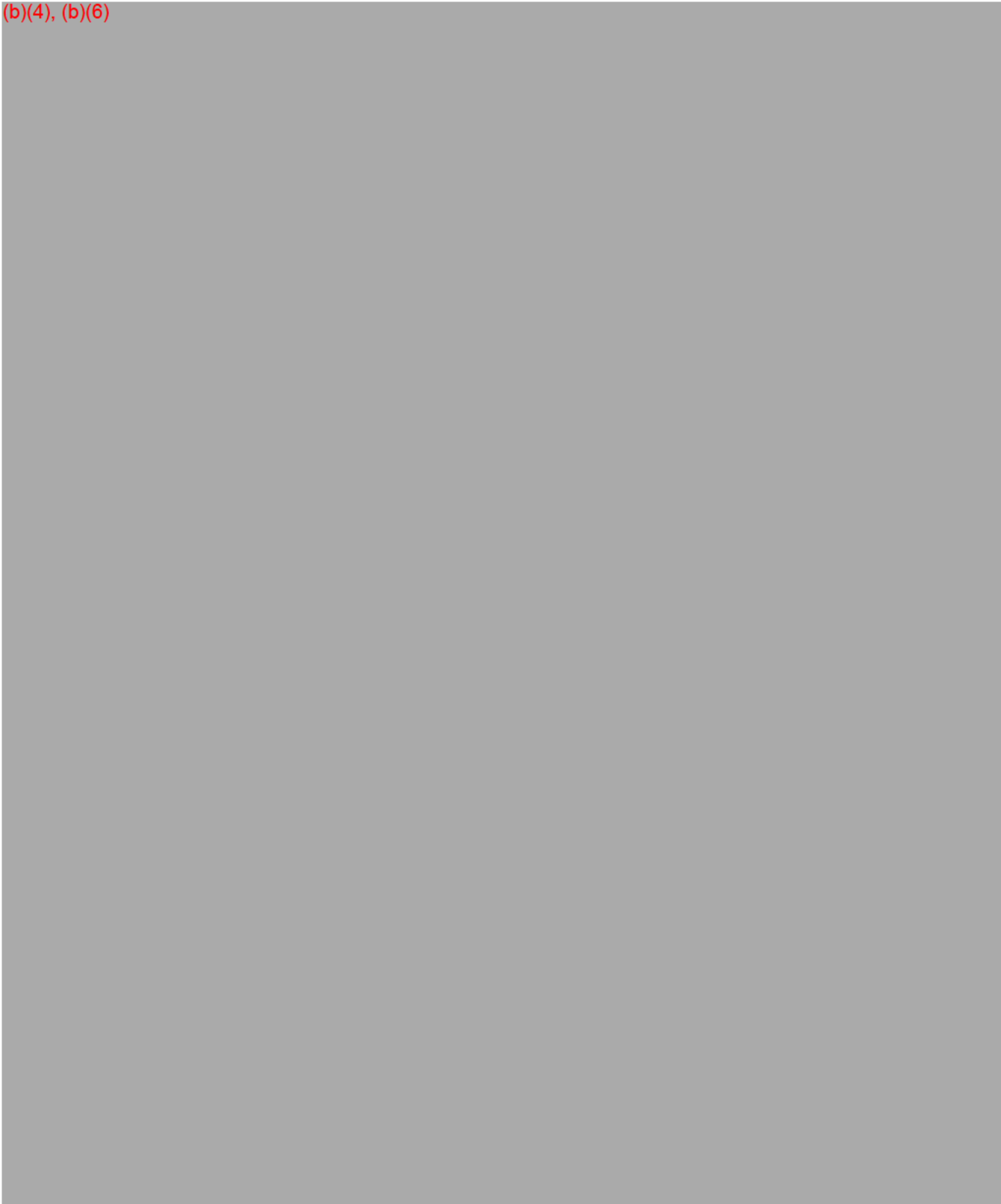
¹³ Pertains only to protocols covering the Gamma design, the design for which PMA approval is being sought.

¹⁴ The IDE for the Phase II study was originally filed and approved for the Beta design of the device. Therefore, only an IDE supplement was filed with the introduction of the Gamma design.


x-ray to be conducted at the one-year visit instead of the 6-month visit, 4) elimination of the Sed Rate test from the screening visit, and 5) elimination of the hematocrit test from the three-month visit.

The 4 and 5 month visits were eliminated, since it was believed that the 3 and 6 month follow-up time points were adequate to cover the first 6 months, and that monthly visits between months 3 and 6 were unduly burdensome. The use of ultrasound to evaluate device location and retention was eliminated since some Investigators reported that it was inadequate in providing a precise enough evaluation of device location. Instead, the HSG already performed at the 3-month visit would be used to evaluate device location, and pelvic x-ray would be used to evaluate device location after the 3-month visit. The pelvic x-ray was moved to the one-year visit to provide this evidence of device retention at a longer-term follow-up time point. The Sed Rate test was eliminated from the screening procedures because the Investigators believed that the test was non-specific and that the results were not useful for determining patient eligibility. Lastly, the hematocrit test was eliminated from the three-month visit because Investigators also reported that it was a non-specific test that did not provide useful information about device wearing.

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March 2001

The Phase II protocol was revised in March 2001, at all sites, to align the requirements of the Phase II protocol with the Pivotal Trial protocol.

These changes are as follows:

1. The long-term follow-up was extended from two years to five years.
2. Wording was modified to describe the patient's responsibility to inform the Investigator about any planned intrauterine procedure or extirpative surgery of the reproductive organs. These modifications were made so that the wording in the Phase II protocol was consistent with the wording requested by FDA for the Pivotal Trial protocol.
3. The Protocol for Managing Patients Who Have Experienced Device Expulsion or Migration (Appendix B of the Phase II protocol) was replaced by the version that was updated for the Pivotal Trial.

In summary, we do not believe that any of the protocol changes over time, nor any of the differences in protocols between sites, impacted the overall study design or endpoints.

EXHIBIT D: INFORMED CONSENT

EXHIBIT E: CASE REPORT FORMS

EXHIBIT F: STUDY DEVIATIONS

EXHIBIT F. STUDY DEVIATIONS

Deviations that occurred from the time period of patient screening through the 36-month post-alternative contraception visit are divided into six categories. A summary of the deviation categories is provided below in **Table 1**.

Monitoring of the study was detailed and thorough, and included write-ups of any deviation noted, even if minor in nature. In this Exhibit is a detailed listing of every deviation. The vast majority of deviations represent a lack of detailed compliance with the protocol and do not impact the study data or conclusions, or patients' rights, safety or welfare.

Table 1. Deviation Report

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EXHIBIT G: DATA TABLES

The attached data tables reference "STOP 07" and "STOP10", which are both protocol numbers that refer to the Phase II Study. The difference in protocol numbers is due to administrative reasons. Included in this Exhibit are updated tables for the wearing and effectiveness follow-up visits (6,12, 18, 24 and 36 months) and the listing of adverse events. All other tables for screening and device placement, and the 3 month follow-up visit can be found in the April 9, 2002 submission of Module V of the PMA.

STOP 07/10
Adverse Events

Study	Patient Number	Adverse Event	Start Date	Start Date Continuing	Start Time	Stop Date	Stop Date Continuing	Stop Time	Severity	Relationship to Study Device	Treatment Required	Other Treatment
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Section I. Clinical Data Report: Pivotal Trial

A. Executive Summary

Introduction

Provided in this introductory section is a description of the unintended pregnancy and abortion rates in the United States as well as the complications associated with pregnancy, the documented need for contraceptive alternatives, a discussion of the risks associated with current methods of permanent birth control (female sterilization), and the unique characteristics of the Essure System for Permanent Birth Control.

Unintended Pregnancy/Abortion Rates

Unintended pregnancy is a significant public health issue that affects not only the woman involved, but also society as a whole. The significance of this public health need is evidenced by the signing into law of Title X of the Public Health Service Act, which provides for a comprehensive federal program devoted entirely to providing family planning services on a national basis.

Using data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, it has been estimated that almost half (48%) of all pregnancies in the United States in 1994 were unintended, and 54% of these ended in abortion¹. In 1994 alone, there were an estimated 3,000,000 unintended pregnancies, with an estimated half (48%) of women aged 15-44 having had at least one unplanned pregnancy sometime in their lives¹. Although teenagers have the highest rate of unintended pregnancy,

¹ Henshaw SK. Unintended Pregnancy in the United States. *Family Planning Perspectives*, 1998, 30(1): 24-29 & 46.

the second highest rate is found in women aged 40-44². Furthermore, the rate of unintended pregnancies in the U.S. has declined little over the past several decades, and remains higher than other developed nations².

In 1997, over one million abortions were performed, and an estimated 43% of women will have at least one abortion by the time they are 45 years old¹.

Abortion is not just an issue that faces teenagers. In fact, based on a 1994-1995 national survey of almost 10,000 abortion patients, over 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women who were age 30 or over³.

Maternal Risks of Pregnancy

According to the CDC⁴, approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Two to three women die each day from a pregnancy-related complication, and the maternal mortality rate has not declined since 1982⁴. The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy. It should be noted that the risk of pregnancy-related death rises after the age of 35⁵. In addition to mortality resulting from pregnancy, the CDC states that more than one in three pregnant women in the U.S. develop a pregnancy-related complication⁴. The most common complications include: miscarriage, ectopic pregnancy, hemorrhage, infection, diabetes, high blood pressure, excessive vomiting, premature labor, need for Caesarean delivery, and depression. Furthermore, based on 1986-1987 data from the National Hospital Discharge Survey (NHDS), an estimated 22.2 per 100 hospitalizations involving a birth were non-delivery

² Global Health Options.

³ Henshaw SK. Abortion Patient in 1994-1995: Characteristics and Contraceptive Use. *Family Planning Perspectives*, 28: 140-147 & 158, 1996.

⁴ CDC's Reproductive Health Information Source. *Safe Motherhood: Promotion Health for Women Before, During, and After Pregnancy* 2002.

⁵ CDC Press Release: Fact Sheet, Pregnancy-Related Mortality.

related hospitalizations of pregnant women⁶. Hospitalization for a pregnancy-related complication required an average of >2 million hospital days of care per year and cost >1 billion dollars annually⁶. The authors of this study provided a nationwide estimation of serious pregnancy-related morbidity following childbirth: 62,400 readmissions occurred during the postpartum period, yielding an average annual rate of 8.1 readmissions per 1,000 deliveries.

As stated by the CDC, childbirth remains the most common reason for hospitalization in the U.S., and complicated pregnancies result in more costly hospitalizations. Thus, since women who have unintended pregnancies are less likely to have appropriate prenatal care, more likely to have entry into prenatal care at a later stage of the pregnancy, and are at an increased risk of domestic violence⁷, they are presumably at higher risk of complications and account for more costs related to pregnancies.

Risks to Infant/Child

The National Commission to Prevent Infant Mortality has stated that: "Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception."⁸ Similarly, a review by the U.S. Institute of Medicine of the research on this topic concluded that "the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development⁹. The CDC also states that an infant from an unintended pregnancy has an increased risk of low birth rate, neonatal mortality, risk of SIDS, and developmental problems⁷.

Clearly, there is a significant public health issue represented by these facts and figures.

⁶ Franks AL. Hospitalization for pregnancy complications, United States, 1986 and 1987. *Am J Obstet Gynecol* 1992; 166:1339-44.

⁷ Koonin LM. Promoting Healthy Pregnancies: Counseling and Contraception. September 20, 2000.

⁸ Alan Guttmacher Institute. Title X and the U.S. Family Planning Effort.

⁹ Alan Guttmacher Institute. Family Planning Improves Child Survival and Health. 1998.

Need for Contraceptive Alternatives

Based on data from the 1995 National Survey on Family Growth, it has been suggested in the literature that the high rates of unintended pregnancy reflect dissatisfaction with current methods¹⁰. In addition, based on a 64-country survey, it has been shown that the prevalence of contraceptive use rises with increased access to a variety of contraceptive methods¹¹.

The 1995 National Survey on Family Growth provided data on the current profile of contraceptive use in the United States based on a survey of almost 7,000 women. The survey revealed that the percentage of women discontinuing contraceptive use for method-related reasons within 12 months of method initiation was 44%¹⁰. In addition, during the lifetime of a typical woman who uses reversible methods of contraception, she will discontinue use for a method-related reason 9.5 times. If women using sterilization are included as well, the typical woman will discontinue use of a contraceptive for a method-related reasons only 7.2 times during her lifetime. The survey also found that the typical woman will experience 1.8 unintended pregnancies. If women using sterilization are included as well, the typical woman will experience 1.3 unintended pregnancies. The survey also noted that 6% of sexually active women were not using a contraceptive, which translates to approximately 3.5 million women at risk of unintended pregnancy. Indeed, of the 6 million pregnancies that occurred that year, nearly half were unintended, and more than half of these unintended pregnancies occurred among women who were using contraceptives.

The need for contraceptive alternatives has been acknowledged in recent years not only in the published literature, but also at meetings of the FDA's OB/GYN

¹⁰ Trussel J. Contraceptive Failure, Method-Related Discontinuation and Resumption of Use: Results from the 1995 National Survey of Family Growth. *Family Planning Perspectives*, 1999, 31(2): 64-72 & 93.

¹¹ Ross J. Contraceptive Method Choice in Developing Countries. *International Family Planning Perspectives*, 2001, 28(1): 32-40.

Advisory Committee. Additionally, the need for less invasive transcervical methods of sterilization has been a primary research focus for the USAID Office of Population, Family Health International (FHI), the CONRAD Program, and the WHO Human Reproduction Program.

In introductory remarks to the panel convened in October of 1996 for the review of the PMA for the Lea's Shield, Mr. Pollard (Chief, Obstetrics and Gynecology Devices Branch, FDA) stated: "I would like to add at this point that FDA is responsive to the concerns of women's advocacy groups across the U.S. Many of these groups are very concerned about the limited number of contraceptive options available to women and believe that FDA should be re-examining its review standards for evaluation of these products. This need for more contraceptive options was most recently emphasized in the report that just issued from the Institute of Medicine entitled 'Contraceptive Research and Development: Looking to the Future', highlighting the high rate of unintended pregnancies in the U.S. and worldwide."

In addition, the FDA convened a meeting of the panel in October of 1999 to discuss the requirements for vaginal barrier contraceptive devices to "recalibrate our premarket entry process and optimize the balance of premarket and postmarket requirements" for these devices, as stated by Mr. Pollard. This was largely driven by the results of the 1995 National Survey on Family Growth. Mr. Pollard presented to the panel some of the results discussed above from the survey regarding high rates of unintended pregnancy, abortion, and discontinuation of contraception due to method-related reasons, and went on to state: "To us, at FDA, that describes a huge unmet need." While the focus of the panel meeting was for vaginal barrier contraceptive devices rather than tubal occlusion devices, the underlying motivation for convening the meeting still pertains to consideration of the Essure System: the large unmet need in the area of contraceptive alternatives for women.

The author of the published findings of the 1995 Survey concluded that the high pregnancy rates in the survey “do not reflect the inherent efficacy of methods when used correctly and consistently, but instead reflect imperfect use because most reversible methods are difficult to use correctly.” The author went on to state: “such high rates of discontinuation almost surely reflect dissatisfaction with current methods.”

Prevalence of Tubal Sterilization

Currently, women must choose between temporary reversible methods, with all the limitations discussed above, and permanent birth control (sterilization), with its attendant invasiveness, morbidity, and mortality. Discussed below is the prevalence of tubal sterilization as a contraceptive choice, as well as the risks associated with this method.

Tubal sterilization is the most prevalent method of birth control in the United States. From 1994-1996, more than 2,000,000 tubal sterilizations were performed, for an annual incidence of 11.5 per 1,000 women, or 684,000 per year¹². As noted by Dr. Carolyn Westhoff at a recent meeting on transcervical sterilization sponsored by ARHP, this may well be an underestimate due to the difficulty in capturing the data in recent years.

All currently approved methods of tubal sterilization require access to the peritoneal cavity, and therefore carry the inherent risk associated with invasive surgery. Half of the tubal sterilizations are performed immediately post-partum and are done via mini-laparotomy or laparotomy¹³. The other half represent “interval” sterilizations, 89% of which are done laparoscopically¹³. Therefore, a slight majority of tubal sterilizations are performed by mini-

¹² MacKay AP. Tubal Sterilization in the United States, 1994-1996. *Family Planning Perspectives*, 2001, 33(4):161-166.

¹³ ACOG Technical Bulletin #222 – April 1996. Sterilization.

laparotomy/laparotomy. Currently, laparoscopy is predominantly performed with general anesthesia and involves one or more punctures of the abdominal wall for insertion of a laparoscope; the tubal ligation procedure is then performed through the puncture sites in the abdomen. Both laparotomy and mini-laparotomy are more extensive procedures and require relatively longer recovery periods than laparoscopic methods. About 93 percent of the procedures in the U.S. are performed in a hospital or surgi-center under general anesthesia, with laparoscopic procedures requiring an average of 4-5 hours of hospital recovery time¹⁴, an average of 4-6 days before returning to regular activities, not including the day of surgery^{15,16}, and an average of 3 days before returning to work¹⁶. For procedures performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

Risks with Tubal Sterilization – Mini-Laparotomy/Laparotomy

The Centers for Disease Control and Prevention (CDC) CREST study¹⁸ reported on a subgroup of almost 300 women who underwent interval tubal sterilization by laparotomy. In this subgroup, a major complication rate of 5.7% was reported¹⁷, which was comprised of febrile morbidity and re-hospitalizations. Re-hospitalization occurred for the following reasons: pelvic abscess, pulmonary abscess, pulmonary embolus, bowel obstructions, staph wound infection at site of laparotomy incision, etc. The mean length of postoperative hospital stay was increased by 1.9 nights for women who had at least one complication as compared to those without complication¹⁷. This does not include the additional

¹⁴ Bordahl PE. Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study. *Obstet Gynecol* 1993; 81: 137-41.

¹⁵ Fraser RA. The prevalence and impact of pain after day-care tubal ligation surgery. *Pain* 39 (1989) 189-201.

¹⁶ Garcia FA. Economic and Clinical Outcome of Microlaparoscopic and Standard Laparoscopic Sterilization, A Comparison. *J Reprod Med* 2000; 45:372-376.

¹⁷ Layde PM. Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy. *Obstet Gynecol* 62:180, 1983.

¹⁸ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-70.

hospitalization experienced by women who were readmitted following their initial discharge. The mean total convalescence period from the time of the surgery until the resumption of normal activities was increased by 8.3 days (from 9.6 days) among women experiencing a complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparotomy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (1.8%), primary incision complications (12.6%), infections (1.1%), and "other" (3.3%). The total complication rate in this study, for the complications reported, was 18.8%. In a similar study comparing the Filshie Clip with the Tubal Ring under laparotomy²⁰, the following complications were noted: surgical injuries (7.3%), primary incision complications (13.9%), infections (0.9%), and "other" (1.4%). The total complication rate in this study, for the complications reported, was 23.5%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional approach.

Risks with Tubal Sterilization – Laparoscopy

Based on data from the CREST study involving over 9,000 women who underwent tubal sterilization by laparoscopy, major complications occurred at a rate of 1.6%, with unintended laparotomy as the most frequent complication²¹. Laparotomies were performed for the following reasons: unexpected bleeding, hematoma formation, viscous perforation (stomach and bowel), and fallopian tube resection. Rehospitalization occurred for the following reasons: pelvic infections, heavy vaginal bleeding, abdominal/pelvic pain, urinary tract infection,

¹⁹ Dominik R. Two Randomized Controlled Trials Comparing the Hulka and Filshie Clips for Tubal Sterilization. *Contraception* 62 (2000) 169-175.

²⁰ Sokal D. Two Randomized Controlled Trials Comparing the Tubal Ring and Filshie Clip for Tubal Sterilization. *Fertility and Sterility*. Vol 74, No 3, September 2000.

²¹ Jamieson DJ. Complications of Interval Laparoscopic Tubal Sterilization: Findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol* 2000; 96:997-1002.

peritonitis caused by bowel burn, bowel obstruction, etc. In an early report based on the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, the median postoperative hospital stay increased from 0 nights for women with no complications to 2 nights for women who had at least 1 complication²². The occurrence of a complication also increased the median total convalescence from 4 days to 14 days. More than one third (36%) of women who developed a complication had a total convalescence longer than 21 days, compared to only 2% of women with no complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparoscopy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (0.8%), primary incision complications (7.9%), infections (0.08%), and "other" (2.5%). The total complication rate in this study, for the complications reported, was 11.2%. In a similar study comparing the Filshie Clip with the Tubal Ring via laparoscopy²⁰, the following complications were noted: surgical injuries (2.2%), primary incision complications (4.4%), infections (0.4%), and "other" (1.0%). The total complication rate in this study, for the complications reported, was 8%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional method.

Finally, a large prospective study involving over 24,000 women who underwent tubal ligation using one of 5 methods²³ was conducted. In this study, the rate of surgical difficulties, which included anesthesia and equipment problems, etc., ranged from 2.4% to 12.5% (5.1% overall). The rate of surgical complications, which included uterine perforation, bowel injury, artery/vein injury, bladder injury, ovarian injury, etc., ranged from 0.7% to 2.7% (1.7% overall). The rate of

²² Destefano F. Complications of Interval Laparoscopic Tubal Sterilization. *Obstet Gynecol* 61:153, 1983.

²³ Bhiwandiwala PP. A Comparison of Different Laparoscopic Sterilization Occlusion Techniques in 24,439 Procedures. *Am J Obstet Gynecol* 144:319, 1982.

technical failures, which required a change to a different technique or abandoning the procedure, ranged from 0.6% to 1.0% (0.8% overall).

Risks of Tubal Sterilization – Local vs. General Anesthesia

Based on early reports of the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, a fivefold difference in complication rates was found between procedures performed under general anesthesia and those performed under local anesthesia²². In subsequent reports from the CREST study involving over 9,000 women, use of general anesthesia was found to be a predictor of complications in women undergoing interval laparoscopic tubal sterilization²¹. In addition, 40% of the deaths attributable to tubal sterilization followed complications associated with general anesthesia, and there were no deaths due to complications from local anesthesia²⁴.

In a randomized, controlled trial comparing tubal ligation performed under local anesthesia to general anesthesia in 125 women, total procedure/post-surgery time was significantly shorter in the local anesthesia group¹⁴. In addition, the general anesthesia group had significantly more abdominal pain during the hospital stay, and use of analgesics immediately after surgery was more extensive. Also, the “awakeness” score was higher in the local anesthesia group the same evening as the procedure. Similar to these findings, in another randomized study comparing laparoscopic tubal ligation performed under local vs. general anesthesia²⁵, women in the local anesthesia group had a slightly shorter anesthesia time and recovery room stay. In addition, women in the general anesthesia group were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate of 110 or higher.

²⁴ Peterson HB. Deaths Attributable to Tubal Sterilization in the United States, 1977 to 1981. *Am J Obstet Gynecol* 146:131, 1983.

²⁵ Peterson HB. Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study. *Obstet Gynecol* 70:903, 1987.

Although use of local anesthesia for tubal sterilization is associated with a lower rate of complications, laparoscopic tubal sterilization still requires access to the peritoneal cavity with its associated risks.

Tubal Sterilization Risks – Pain/Return to Normal Activities

Finally, in a study of over 50 women using validated measures to assess the incidence, intensity and duration of pain following tubal ligation performed laparoscopically, it was found that 85% of women reported that pain and/or fatigue impacted their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of the procedure. The most powerful predictor of return to normal activity was the total amount of pain experienced. A separate study of 50 women undergoing laparoscopic tubal sterilization similarly found that the average number of days to resume normal activities was 4-6¹⁶. Also, as stated above, when tubal sterilization is performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

A New Contraceptive Alternative – The Essure System

Given the high unintended pregnancy, abortion and discontinuation rates associated with temporary methods of birth control, and the significant complications that can occur with the invasive surgery currently required for permanent birth control, we believe that women would benefit from a new contraceptive alternative that offers a less invasive method to achieve permanent birth control. As evidence of patient interest in such an alternative, is the statement made by a patient advocacy group to the FDA's OB/GYN Advisory Committee (panel). In February of 1996, Ms. Cindy Pearson, Program Director of the National Women's Health Network addressed the panel, which was convened to review the PMA for the Filshie Clip, stating: “. . . So we just wanted

to communicate a general sense that women are interested in alternative methods of sterilization. In particular, women are interested in methods that offer a safety or convenience advantage over the methods that are currently available to them.”.

The Essure System offers transcervical placement of the Essure Micro-insert, which can be accomplished without incisions or general anesthesia, with no loss of method effectiveness as compared to incisional tubal sterilization. Since the data that follow in this report demonstrate that this can be done safely and effectively to provide permanent birth control, we believe that this alternative will be embraced by women and their physicians, and will offer a significant public health benefit as a result.

Summary

In summary, due to the following points, we believe that there is strong evidence of the need for a new contraceptive alternative for women, especially a permanent method that can be performed without incisions or general anesthesia:

- An estimated half (48%) of pregnancies that occur in the United States each year are unintended, translating to an estimated 3,000,000 unplanned pregnancies in the United States each year.
 - The age group that has the second highest rate of unintended pregnancy is women aged 40-44.

- An estimated half of all unintended pregnancies result in abortion, translating to an estimated 1,000,000 abortions each year in the United States.
 - 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women over 30 years old.

- The morbidity associated with pregnancy is not infrequent or insignificant to the women or to society.

- There has been a documented risk to infants and children due to unintended pregnancies.
- Deaths and major complications occur with currently available methods of tubal sterilization due to general anesthesia and invasion of the peritoneal cavity that is associated with current methods.

We believe that many of the unintended pregnancies and abortions each year could be avoided if women had a permanent birth control option with an alternative risk/benefit profile than current methods.

Executive Summary of Clinical Data

Detailed data on the Pivotal Trial conducted to establish a reasonable assurance of safety and effectiveness for the Essure System are provided in the following sections. This section provides an Executive Summary of the data.

Protocol

Women in this study were followed at the following time points:

- One week-post device placement (PDP)
- 3-months PDP
- 3, 6, and 12 months post-alternate contraception (PAC)
- 18 months to 5 years as part of a Post-approval Study.

This figure provides an overview of the clinical trial visits.

(b) (4)



Placement Rates

Of the 518 women in the initial Intent-to-Treat group, 464 (89.6%) achieved bilateral placement; 446 (86.1% on the first procedure and 18 (3.5%) after a second procedure). Of the 507 women in the Device Evaluation Group, bilateral placement was achieved in 464 (92%) (446 (88.0%) on the first procedure and 18 (3.6%) after a second procedure), and single Micro-insert placement was achieved in the 2 women with a unicornuate uterus (100%). Of the 41 women (8%) with bilateral tubes who did not achieve bilateral placement, 15 (37%) were found to have proximal tubal occlusion (PTO) on follow-up HSG. Eliminating these women from the analysis of placement rates results in an overall bilateral placement rate of 464/492 (94%).

Satisfactory Micro-Insert Location/Occlusion Rates

A total of 456/464 women (98%) with bilateral placement completed the 3-month post-device placement visit and underwent an HSG. Of those 456 women, 437 (96%) were noted on HSG to have Micro-inserts in satisfactory location. Of those 437 women, 421 (96%) were also noted to have bilateral tubal occlusion. Nine of the 19 women with Micro-inserts in unsatisfactory location returned for a second placement procedure to replace an expelled Micro-insert. All achieved bilateral placement and were found on follow-up HSG to have bilateral occlusion and Micro-inserts in satisfactory location. All of the 16 women who had tubal patency at the initial HSG chose to undergo a second HSG 3 months later, and all were found to have bilateral occlusion on the second HSG. Therefore, of the 456 women with bilateral placement completing the 3-month visit, 446 (98%) were ultimately found to have Micro-inserts in satisfactory location and bilateral occlusion. In addition, 100% (446/446) of the women with Micro-inserts in satisfactory location ultimately had bilateral occlusion.

Reliance Rates

As stated above, 446/456 women (98%) with bilateral placement completing the 3-month PDP visit were able to rely on Essure for contraception. In addition, 3 women with bilateral placement did not have an HSG but chose to begin relying on Essure. Also, four women with unilateral placement and either confirmed contralateral PTO (2) or a unicornuate uterus (2) were able to rely on Essure for contraception. Therefore, among the 507 women in the Device Evaluation Group, 453 (89%) were ultimately able to rely on Essure for contraception, and among the women with bilateral placement, 449/464 (97%) were ultimately able to rely on Essure for contraception. These percentages are conservative since they count lost-to-follow-up women as "not relying".

Adverse Event Rate

Adverse events on the day of the placement procedure were reported in 16 (3%) women. All events were resolved prior to the woman being discharged from the recovery room, except for one woman who required overnight observation following an adverse reaction to pain medication. Day of procedure adverse events included the following, all of which occurred in <1% of cases: vomiting, vaso-vagal response, hypervolemia, band detachment, excessive vaginal bleeding, and “other” (skin itching, bloating, loss of appetite, and reaction to saline used for uterine cavity distension).

Adverse events that *initially* prevented the woman from relying on Essure occurred in 21 (4.5%) women. These were primarily Micro-insert expulsions following original Micro-insert placement that was out-of-specification. Nine of the women who experienced an expulsion chose to undergo a second placement procedure, and all were successful. Therefore, adverse events that *ultimately* prevented reliance occurred in only 12 women (2.6%). The most frequently reported adverse events reported in the first year (fifteen months PDP) that did not prevent the woman from relying on Essure, but were rated by the Investigator as at least “possibly” related to Essure, were back pain (6.2/1000 women months), abdominal pain/cramps (2.6/1000) and dyspareunia (2.5/1000 women months). All other events occurred at less than 2.5/1000 women months of wearing.

Patient Satisfaction/Comfort

Women in the study consistently rated their overall satisfaction and comfort in wearing the Micro-inserts as very high. One-week post-device placement, >95% of women rated their comfort as “good” to “excellent” and their satisfaction as “somewhat satisfied” to “very satisfied”. At all subsequent study visits, 99% of women rated their comfort with wearing Essure as “good” to “excellent”. At all

study visits, at least 98% of women rated their overall satisfaction as somewhat to very satisfied (this included women who were not able to rely on Essure).

Pregnancy Prevention

There have been no pregnancies in any of the 453 women who have relied on Essure for contraception (449 with bilateral placement). There are 439 women with bilateral placement who have been followed for at least one-year after relying on Essure for contraception and 10 women who began relying on Essure but subsequently were lost-to-follow-up (there are 3 additional women who were lost-to-follow-up prior to the 3-month PDP visit, at which women are told whether they can begin relying on Essure).

There were 4 luteal phase pregnancies reported in the Pivotal trial (pregnancies occurring prior to Essure Micro-insert placement but not detected on the day of placement). None of these 4 women became pregnant while relying on Essure for contraception. Each of the pregnancies in these four women was terminated, and each of the four women was subsequently able to rely on Essure for contraception and has not reported a pregnancy while relying on Essure.

Combined with data from the Phase II study of Essure, this equates with over 636 women-years of first year effectiveness evaluation (and 272 woman-years of second year evaluation). The current estimate of the one-year effectiveness rate based on these combined data is 100% (95% CI 99.53-100%).²⁶

²⁶ One woman in the Phase II trial who received a prior device design (Beta Design of the STOP Device) that was discontinued in 1998 became pregnant after relying on the discontinued design for 2 years. This pregnancy is not included in the Phase II effectiveness calculation since it is a different device than that for which approval is being sought. The device studied in the Pivotal trial is the Gamma version of the STOP device. The Gamma version has been trademarked as "Essure". All prior versions are referred to as "STOP" with a version name: alpha or beta.

Summary

In summary, we believe that the data contained in this Pivotal Trial Report, together with the data provided elsewhere in the PMA, provide a reasonable assurance of the safety and effectiveness of the Essure System based on valid scientific evidence.

B. Background

Four separate studies of the Essure System were conducted as part of the clinical development of the product. Each is depicted in the graphic below.

(b) (4)



The reports of the first 3 studies were included in PMA Module I, Module III and Module V, respectively. Unlike prior clinical trials, the Pivotal Trial included evaluation of the gamma design only.

The IDE for the Pivotal Trial of the Essure System (G000055) was submitted to the FDA on February 28, 2000, following a pre-IDE meeting on November 19, 1999. Conditional IDE approval was received on March 24, 2000, and final IDE approval was received on September 7, 2000.

It should be noted that this report reflects the study protocol and statistical plan that were approved under the IDE. Approximately 10 months after final IDE approval, on June 29, 2001, a Determination/Agreement meeting was held with the Agency to make binding the agreements reached during the IDE approval process. Binding agreement was reached for the majority of the earlier agreements under the IDE. The two exceptions were: 1) filing the PMA if only a 95% effectiveness rate was established, and 2) use of the CREST study as a historical control. Agreement to use the CREST study as a “qualitative benchmark” as opposed to a statistical control group was reached, however.

Because this Report necessarily reports on the approved protocol and statistical plan, it makes reference to use of the CREST study as a historical control and the original 95% effectiveness rate. The 95% effectiveness rate target is now a moot point, as the data support a one-year effectiveness rate that is substantially higher; however, the statistical plan attached is the one approved under the IDE, so it still references the 95% effectiveness rate target.

We provide this background to let the Agency know that we acknowledge the lack of binding agreement on the above two items, and to clarify that this Report necessarily contains and reflects the original IDE approved documents (protocol, statistical plan), since there are no other approved documents to report against.

C. Study Design/Endpoints

The Pivotal Trial of the Essure System (formerly known as STOP) was designed as a multi-center, non-randomized, single-arm, international study of women seeking permanent contraception. The study was conducted in the U.S., Europe, and Australia. The targeted study population was 400 women in whom bilateral Micro-insert placement was achieved. It was expected that more than 400 women would need to be enrolled in order to obtain 400 women in whom bilateral placement was achieved.

The primary endpoints for this study were:

- Prevention of pregnancy;
- Safety of the Micro-insert placement procedure; and
- Safety of the Micro-insert wearing.

The secondary endpoints for this study were as follows:

- Participant satisfaction with the Micro-insert placement procedure;
- Participant satisfaction with Micro-insert wearing;
- Bilateral Micro-insert placement rate; and
- Development of a profile for an appropriate candidate for the Essure procedure.

The study was designed to include 5 years of post-alternative contraception follow-up, 1 year of which was to be completed prior to a PMA filing. The remaining 4 years will be completed as part of a Post-Approval Study. Binding agreement to file the PMA based on one-year follow-up of 400 women has been reached (see letter from FDA dated August 2, 2001, **Exhibit A**). Subsequent to the binding agreement, FDA accepted our proposal to file the PMA with one-year follow-up visits completed on 350 women (see FDA letter dated March 15, 2002, **Exhibit A**).

It should be noted that the study had two phases: 1) the "Post-Device (Micro-insert) placement" (PDP) phase, and 2) the "Post-Alternative Contraception" (PAC) phase. The "Post-Device Placement" phase was the time period between Micro-insert placement and the 3-month visit, during which women were instructed to rely on alternative contraception. At the 3-month visit, a hysterosalpingogram (HSG) was conducted to evaluate Micro-insert location and tubal occlusion. Assuming both were satisfactory, women were instructed to discontinue alternative contraception, thus entering the "Post-Alternative Contraception" (PAC) phase of the study, during which they relied on Essure solely for contraception. If the HSG was not satisfactory, then, depending on the circumstances, women were instructed to either seek alternative contraception or remain in the "Post-Device Placement" (PDP) phase until a second HSG or Micro-insert placement procedure was performed.

D. Clinical Trial Conduct/GCP Compliance Statement

The study was conducted in compliance with Good Clinical Practices (GCPs) – 21 CFR, Parts 50, 54, 56 and 812. All sites conducted the study according to the same protocol as that approved by the FDA (IDE # G000055) and by the Medical Device Authority (MDA) in the United Kingdom. All sites also obtained approval from an Institutional Review Board (IRB)/Ethics Committee (EC) before study commencement.

(b)(4)



E. Clinical Trial Monitoring

(b) (4)



(b) (4)



F. Study Population/Selection Criteria (Inclusion/Exclusion)

Study candidates were women seeking permanent contraception. Permanent contraception candidates were screened for eligibility to participate in this clinical study. Candidates who met the inclusion and exclusion criteria and who were willing to participate in the study were provided with an Informed Consent form for their review and signature prior to screening tests.

The objectives of the inclusion and exclusion criteria were to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

The detailed inclusion and exclusion criteria are provided in the protocol, **Volume 3 of the April 19, 2002 PMA, Exhibit A.**

G. Control Population

(b) (4)



²⁷ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996; 174:1161-70.

²⁸ See Appendix A to February 3, 2000 submission in follow-up to Pre-IDE meeting, as well as Section X of the original IDE application, and Appendix E of August 7, 2000 response to 2nd conditional approval letter.

H. Investigational Sites

(b) (4)



I. Number of Investigators/Number of Subjects per Investigator

(b) (4)



Table 1. Investigators/# Women Scheduled for Micro-insert Placement Procedure

Location	Investigator	Site number	No. Women
(b) (4), (b) (6)			

J. Clinical Protocol

The complete protocol is provided in **Volume 3 of the April 19, 2002 PMA, Exhibit A**. The Informed Consent form for the study is provided in **Volume 3 of the April 19, 2002 PMA, Exhibit B**. The Patient Questionnaires and the electronic Case Report Forms for the study are provided in **Volume 4 of the April 19, 2002 PMA**²⁹. A flowchart of the study sequence can be found below in **Figure 1**, followed by a brief summary of each protocol visit.

Figure 1 Pivotal Trial Protocol

(b) (4)



²⁹ The draft of the CRFs were first submitted on March 10, 2000 in an IDE amendment. The final version was submitted on May 19, 2000 as Exhibit K of the response to the conditional approval letter. The CRFs were further modified to correct for minor discrepancies with the protocol and for functionality with the InForm system. However, these changes did not impact the data that was collected.

Eligibility

The eligibility phase, through screening questions, counseling, and physical exam and labs, was designed to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

Screening

(b) (4)



Micro-insert Placement

Day of procedure activities were to:

- Conduct a pregnancy test, pre-procedure
- Review counseling, pre-procedure
- Perform the Micro-insert placement procedure
- Conduct the pain assessment and satisfaction questions post-procedure
- Conduct the X-ray verification of Micro-insert placement
- Provide post-procedure instructions, covering patient diaries/questionnaires and need for alternative contraception until 3-month PDP visit

(b) (4)



(b) (4)



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K. Study Period

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³⁰ Some women had second device placement procedures that occurred beyond this date. All such procedures occurred by June 2001.

L. Investigational Device Accountability

The Investigational device accountability information is provided in **Exhibit B**.
There was complete accountability for all study devices.

M. Statistical Methods

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N. Patient Tree

(b) (4)



(b) (4)



O. Withdrawn/"Safety Only" Women

(b) (4)



(b) (4)



P. Patient Demographics

(b) (4)



(b) (4)



(b) (4)



Q. Study Deviations

(b) (4)



R. Study Results

(b) (4)



(b) (4)



(b) (4)



Table 9. Reasons for Failed Micro-insert Placement

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(b) (4)



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(b) (4)



(b) (4)



³⁵ See second conditional approval letter dated June 21, 2000, item #34.

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Table 45. Adverse Events Preventing Reliance Among Bilateral Placements

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7. **Effectiveness**

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(b) (4)



Censoring

(b) (4)



(b) (4)



S. Justification for Use of Foreign Data

(b) (4)



T. Conclusions Drawn from the Study

(b) (4)



(b) (4)



(b) (4)



(b) (4)



U. Risk to Benefit Analysis

(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



V. Case Report Forms for Lost to Follow-up Participants

Case Report Forms for lost-to-follow-up women are included in **Volumes 5-7**.

W. Summary Data Tables

Summary data tables for the 6, 12, 18 and 24-month PAC visits, the wearing and effectiveness table, and the adverse event table, based on the data freeze of October 14, 2002, are included in **Volumes 8-10**. Data tables for screening, device placement and the 3 month PDP and 3 month PAC visits were included in the June 5th, 2002 PMA Amendment, Volumes 8-10.

Exhibit A - FDA Correspondence
Binding Agreement (FDA Letter August 2, 2001)
Early PMA Acceptance (FDA Letter March 15, 2002)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

**Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850**

MAR 15 2002

(b)(6)

RECEIVED
MAR 15 2002
BY: _____

Conceptus, Inc.
1021 Howard Avenue
SAN CARLOS CA 94070

Re: M010031 Early Submission of PMA Application for Essure System
Received: December 21, 2001
Amended: February 13, 2002

Dear (b)(6) :

(b) (4)

Page 2 - (b) (6)

(b)(4)



If you have any questions, please call (b) (6)

(b) (6)

Sincerely yours,

(b) (6)



Center for Devices and Radiological Health



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

**Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850**

RECEIVED
AUG 10 2001
BY: _____

AUG 2 2001

(b) [Redacted]
(6) [Redacted]

Clinical Research and Regulatory Affairs
Conceptus, Inc.
1021 Howard Avenue
San Carlos, California 94070

Re: I010178 – 513(a)(3)(D) Determination and 520(g)(7) Agreement Meeting
STOP™ System (Selective Tubal Occlusion Procedure) Device
Received: May 22, 2001
Amended: July 17, 2001

Dear (b) (6) :

(b) (4) [Large Redacted Area]

PMA Amendment
Report of Pivotal Trial: June 5, 2002

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

Page 2 -

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Page 3 - (b) (6)

(b) (4)

The agreement decision is binding on the Center for Devices and Radiological Health. It can be changed only with the written agreement of the sponsor or when there is a substantial scientific issue essential to determining the safety or effectiveness of the device, and only following an opportunity for the sponsor to meet with CDRH to discuss the scientific issue involved. Details of our determination/agreement meeting are enclosed.

If you have any comments or questions regarding this letter, please contact

(b) (6)

Sincerely yours,

(b) (6)

Center for Devices and
Radiological Health

Enclosure

Minutes of Meeting

Participants:

CDRH/FDA

Conceptus, Inc.

(b) (6)



Date: June 29, 2001

(b)(4)



(b)(4)



**PMA Amendment
Report of Pivotal Trial: June 5, 2002**

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

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(b)(4)



(b)(4)



Prepared by: (b) (6) – 7/12/01
Revised: 7/17/01, 7/20/01, 7/23/01, 7/26/01, 7/30/01

PMA Amendment
Report of Pivotal Trial: June 5, 2002


Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

128

Exhibit B - Investigational Device Accountability

Exhibit B - Investigational Device Accountability

(b) (4), (b) (6)



⁵³ 5-day notification dated October 27, 2000; G000055/S8.

(b) (4), (b) (6)

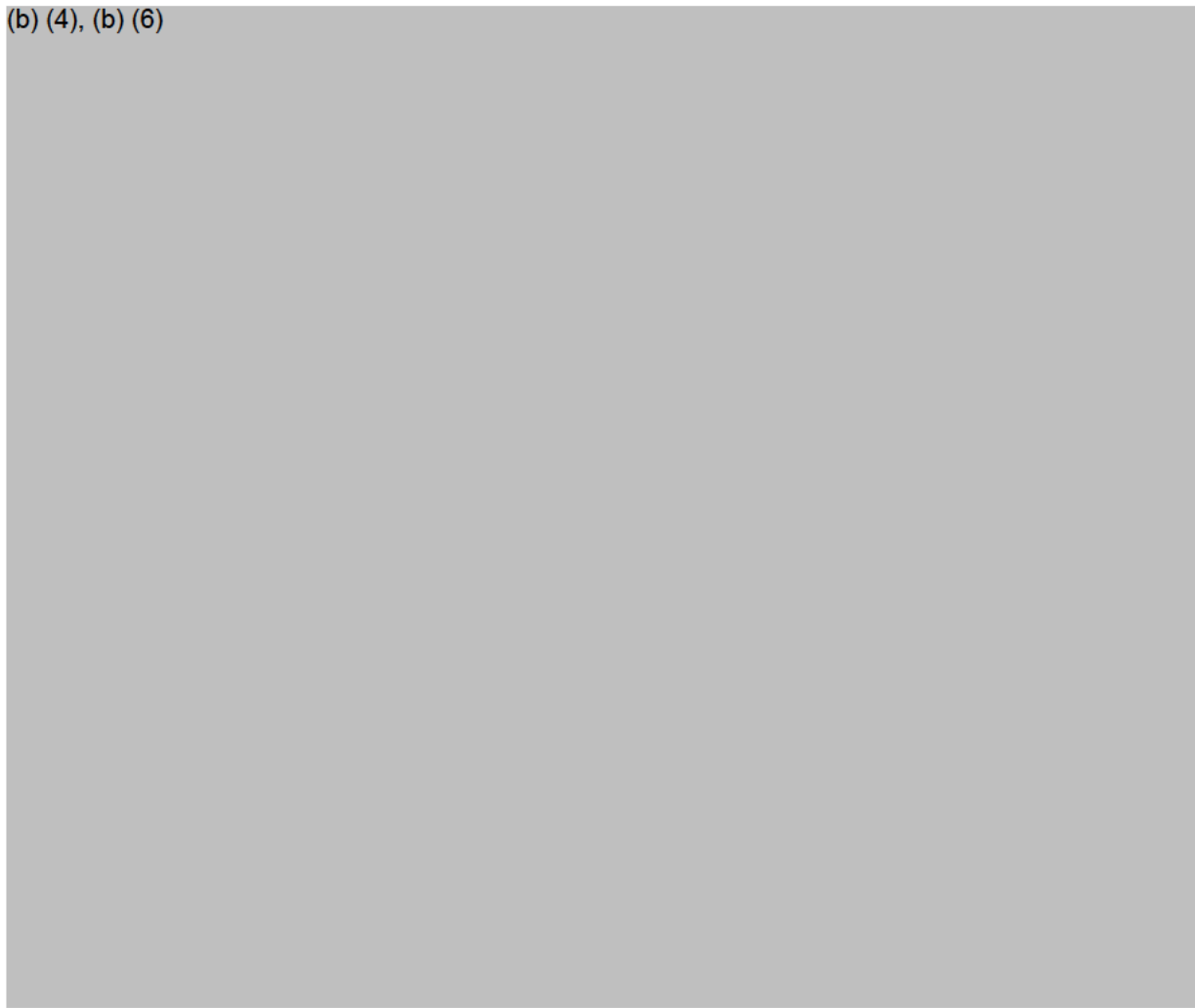


Exhibit C - Study Deviations

Exhibit D - Luteal Phase Pregnancies

Exhibit D - Luteal Phase Pregnancies

(b) (4)



⁵⁴ Wilcox AJ, Baird DD, Dunson D, et. al. Natural limits of pregnancy testing in relation to the expected menstrual period. JAMA Vol 286 No. 14, Oct 10, 2001.

⁵⁵ Peterson HB, et.al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996; 174:1161-70.

⁵⁶ The CREST data was collected at a time when early pregnancy testing was not available. Thus, women who did not have an advancing pregnancy were likely never diagnosed if they had early pregnancy loss. Whereas in our study, women were diagnosed very early and in fact one pregnancy was also spontaneously resolving at the time of diagnosis.

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(b) (6)

A small rectangular grey box redacting a portion of the document.

(b) (4)

A large rectangular grey box covering the majority of the page, indicating a significant redaction of content.

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Exhibit E - Predictors of Placement Failure

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⁵⁷ A woman could have had any of the above outcomes, so the number excluded in the analysis was not the sum of the figures presented.

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Table 2. Demographic variables and placement success

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Exhibit F – Learning Curve Analysis

Exhibit F – Learning Curve Analysis

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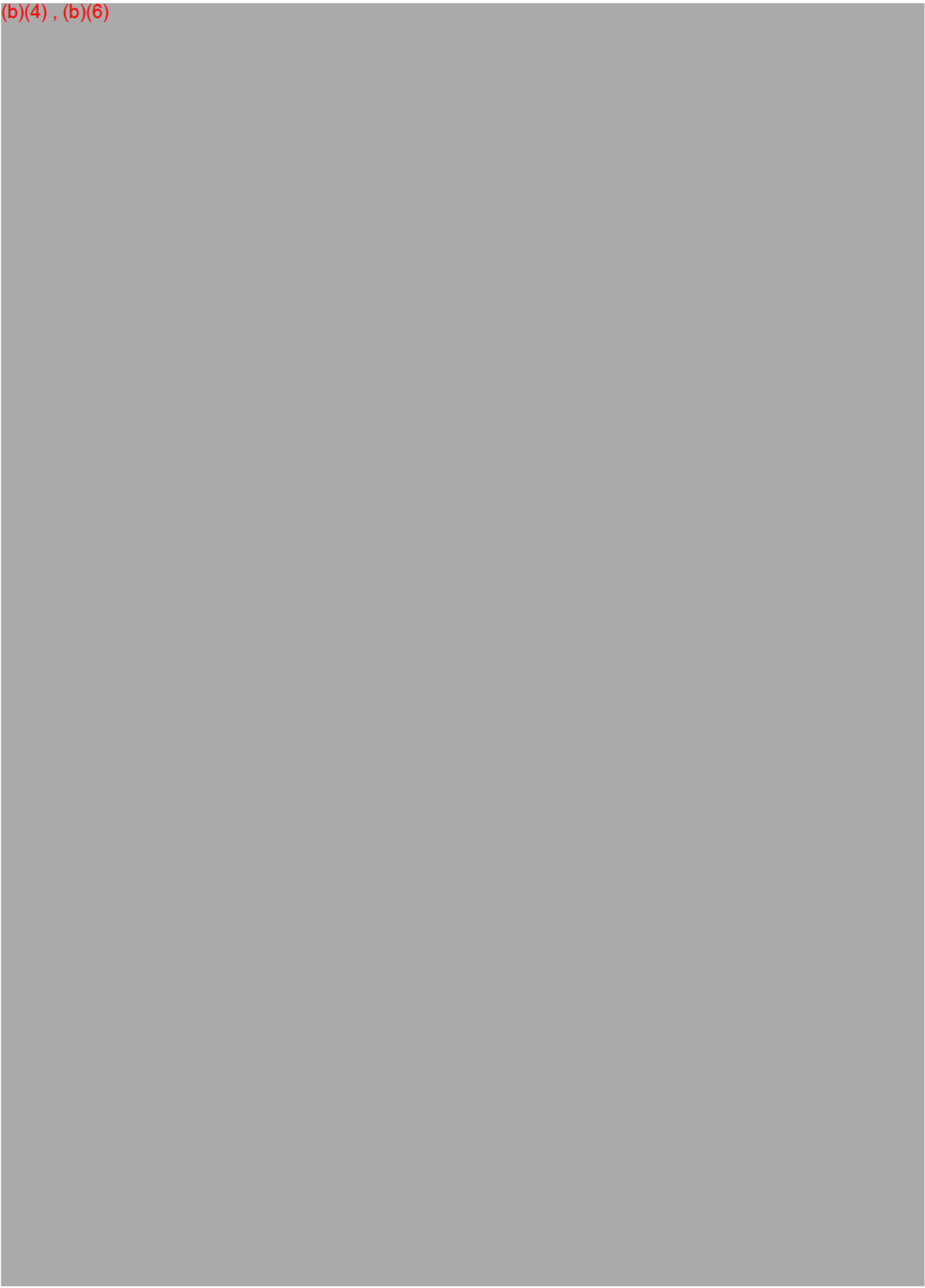
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Exhibit G: Draft Manuscript

**Exhibit H – Histology Picture from Perforated Micro-insert
(b) (6) removed from peritoneal cavity**

(b) (6)



Exhibit I – Censoring Analysis for Effectiveness Calculation

Exhibit I – Censoring Analysis for Effectiveness Calculation

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**Exhibit J - Country-by-Country Analysis of Placement, Adverse
Events Preventing Reliance and Reliance Rates**

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(b) (4)



Exhibit K-

Listings by Site of Adverse Events

Listing by Site of Protocol Deviations


Adverse events by site (Table number refers to Pivotal trial report table number)

Site	Investigator	Subject Number	Table Number	Adverse Event
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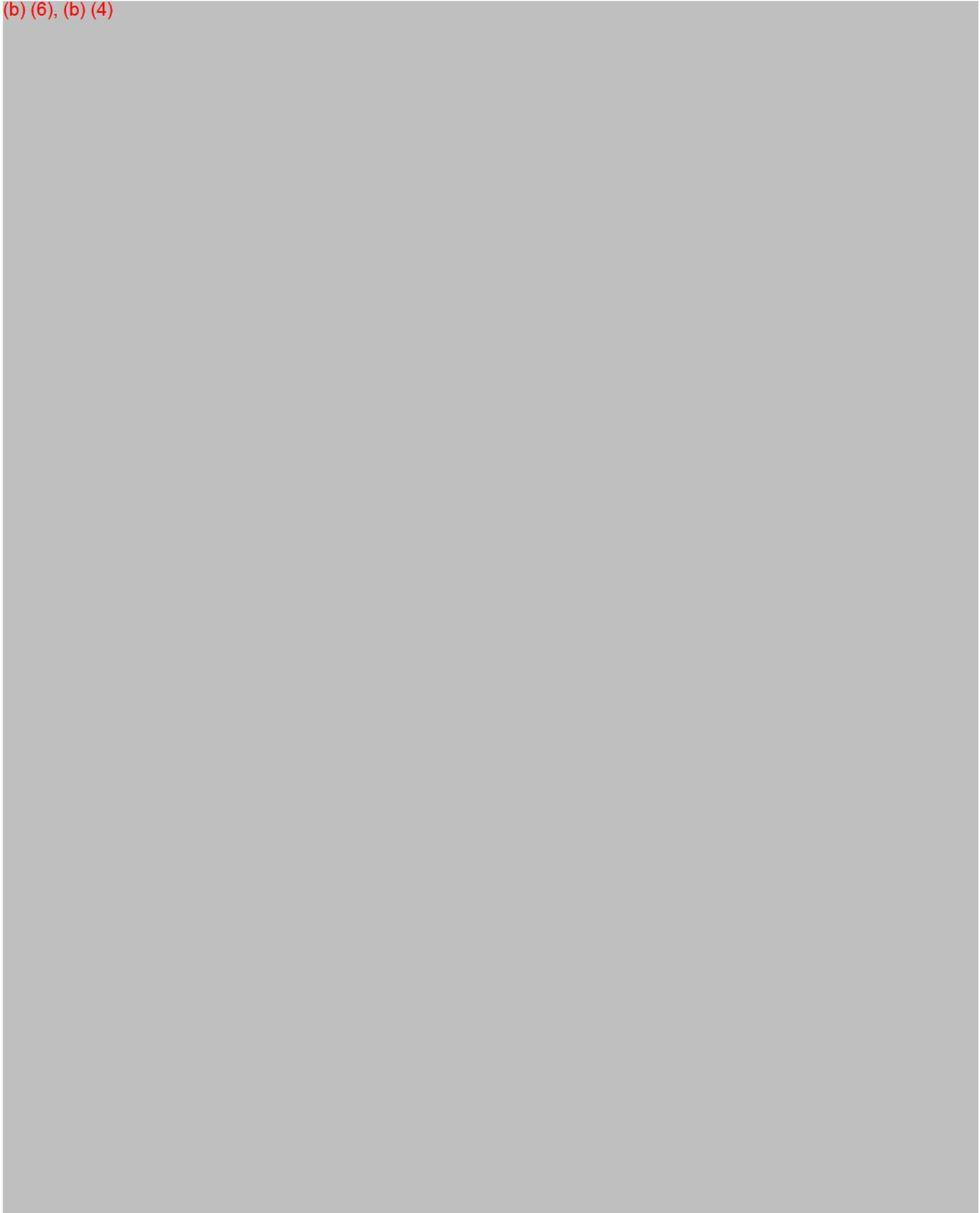
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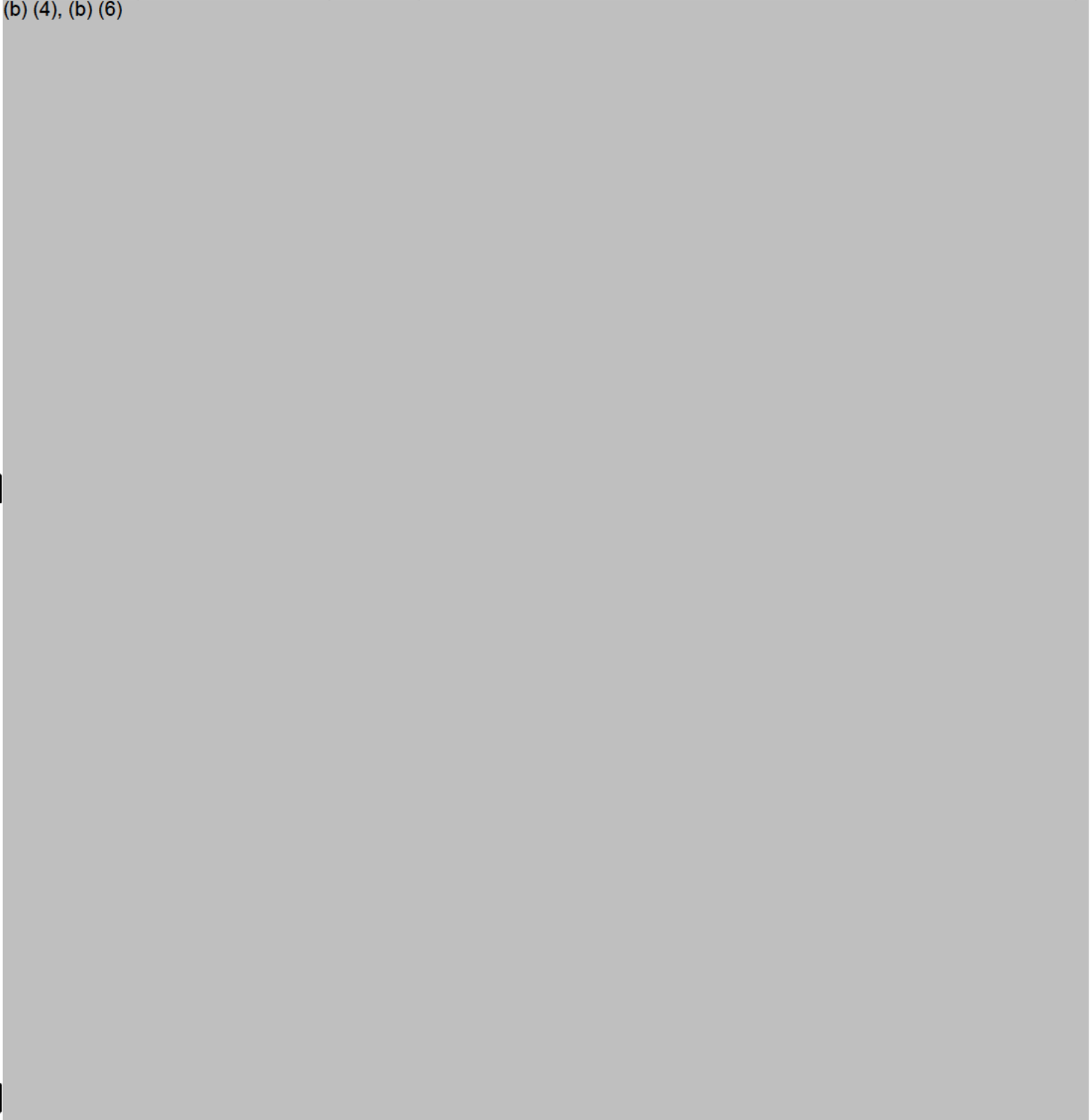
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Deviations by site

Site	Investigator	Subject Number (all are (b) (6))	Description of Deviation
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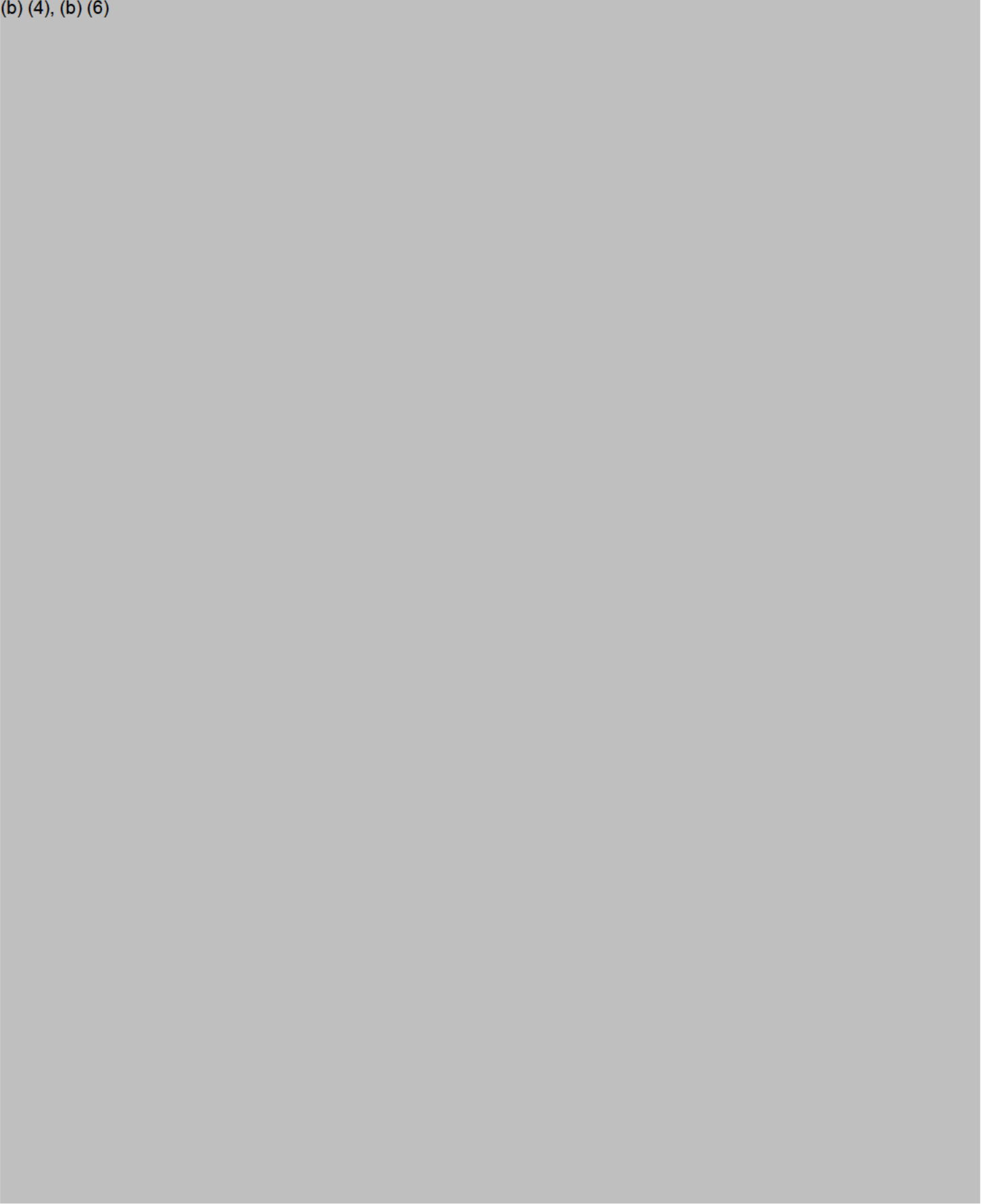
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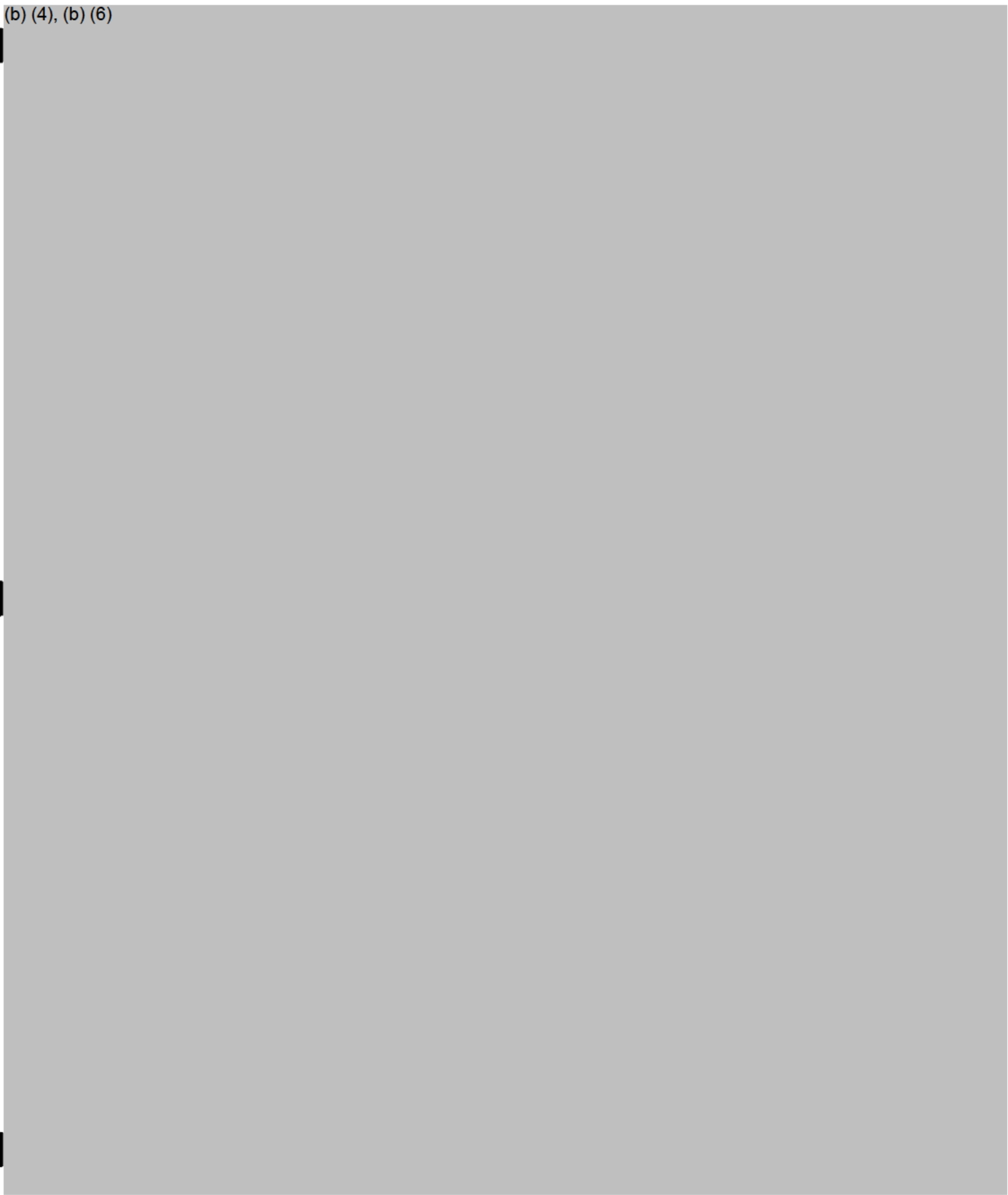
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P020014/P18/C1/V3

PMA Amendment
Conceptus, Inc.

Conceptus Essure™ System

Amendment to PMA No. P020014

Table of Contents

Volume 3 -NOT RECOPIED FOR THIS AMENDMENT. PLEASE REFER TO VOLUME 3 OF APRIL 19, 2002 PMA FOR THE BELOW DOCUMENTS

- Exhibit A** - Study Protocol
- Exhibit B** - Informed Consent Form
- Exhibit C** - Statistical Plan (Final Clean Copy)
- Exhibit D** - Statistical Plan (with Changes Noted)

RECEIVED
 2002 OCT 16 A 10:11
 FDA/CDRH/OCE/PHO

1

P020014/18/C1/V4
PMA Amendment
Conceptus, Inc.

Conceptus Essure™ System
Amendment to PMA No. P020014
Table of Contents

Volume 4 -NOT RECOPIED FOR THIS AMENDMENT. PLEASE
REFER TO VOLUME 4 OF APRIL 19, 2002 PMA FOR THE BELOW
DOCUMENTS

- Exhibit A - Patient Questionnaires**
- Exhibit B - Electronic Case Report Forms**

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(b)(4), (b)(6)-Patient Questionnaires

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Visit: Screening

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Visit: Device Placement1

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RECEIVED

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FDA/CDRH/OCE/PMO

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RECEIVED

STOP 2000 Adverse Events up to 1 Year

Subject Number	Subject	Visit	Adverse Event	Date of	Date	Severity	Relationship	Event	Treatment	Outcome		
	Event			Onset	Resolved		to Study Device	Unanticipated	Required	Recovered Without Treatment	Recovered With Treatment	Other

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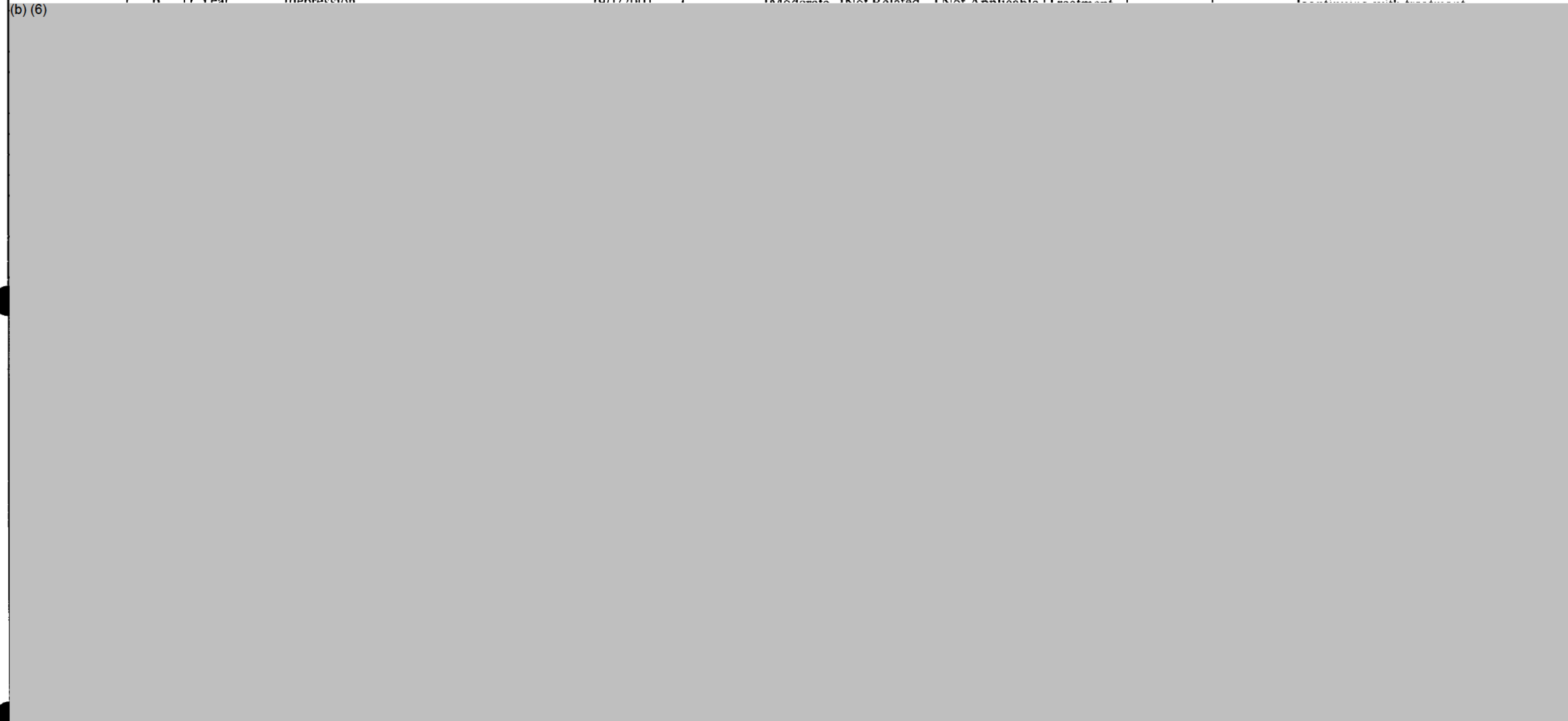


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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
(b) (6)	6	1 Year	depression	0/1/2001		Moderate	Not Related	Not Applicable	Treatment			continuing with treatment



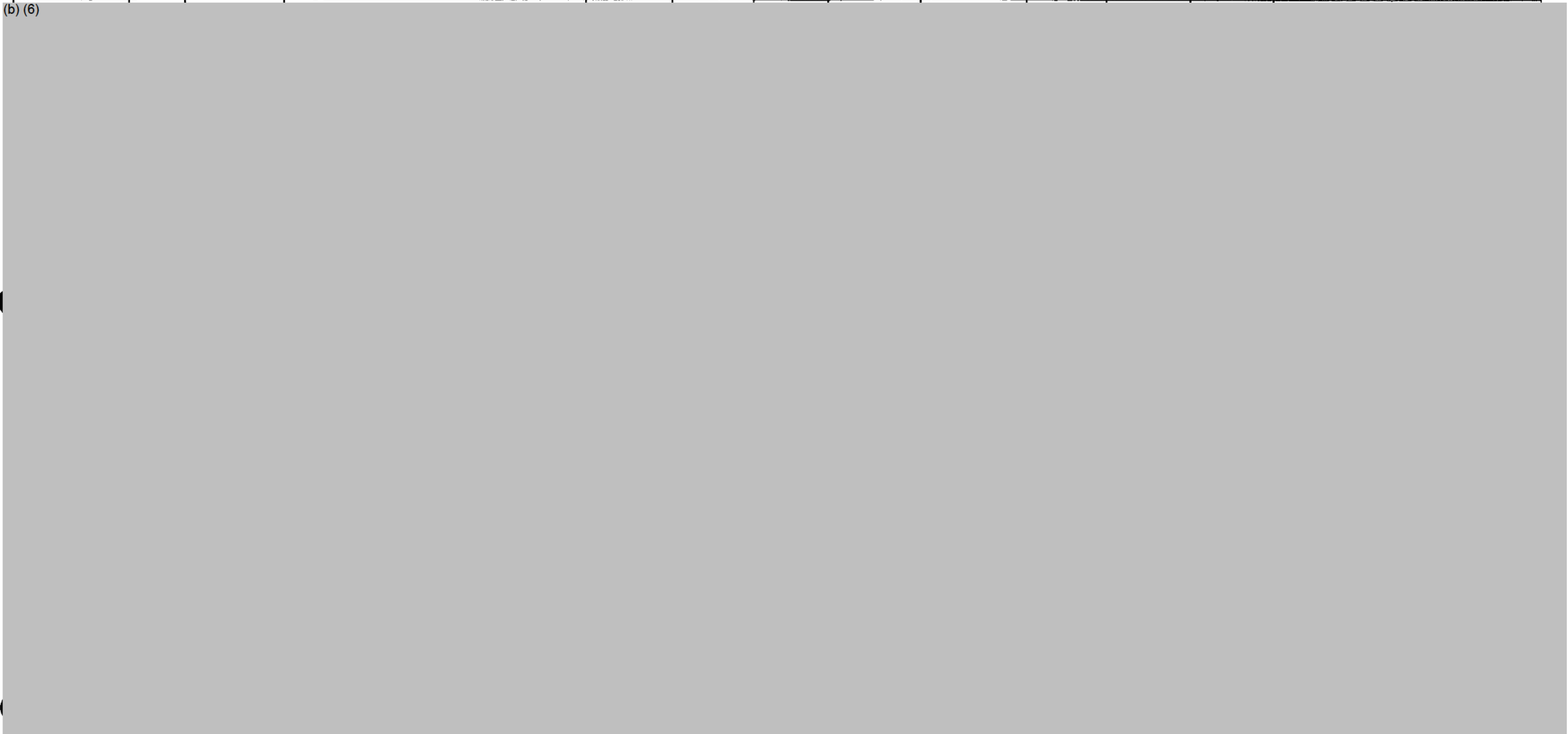
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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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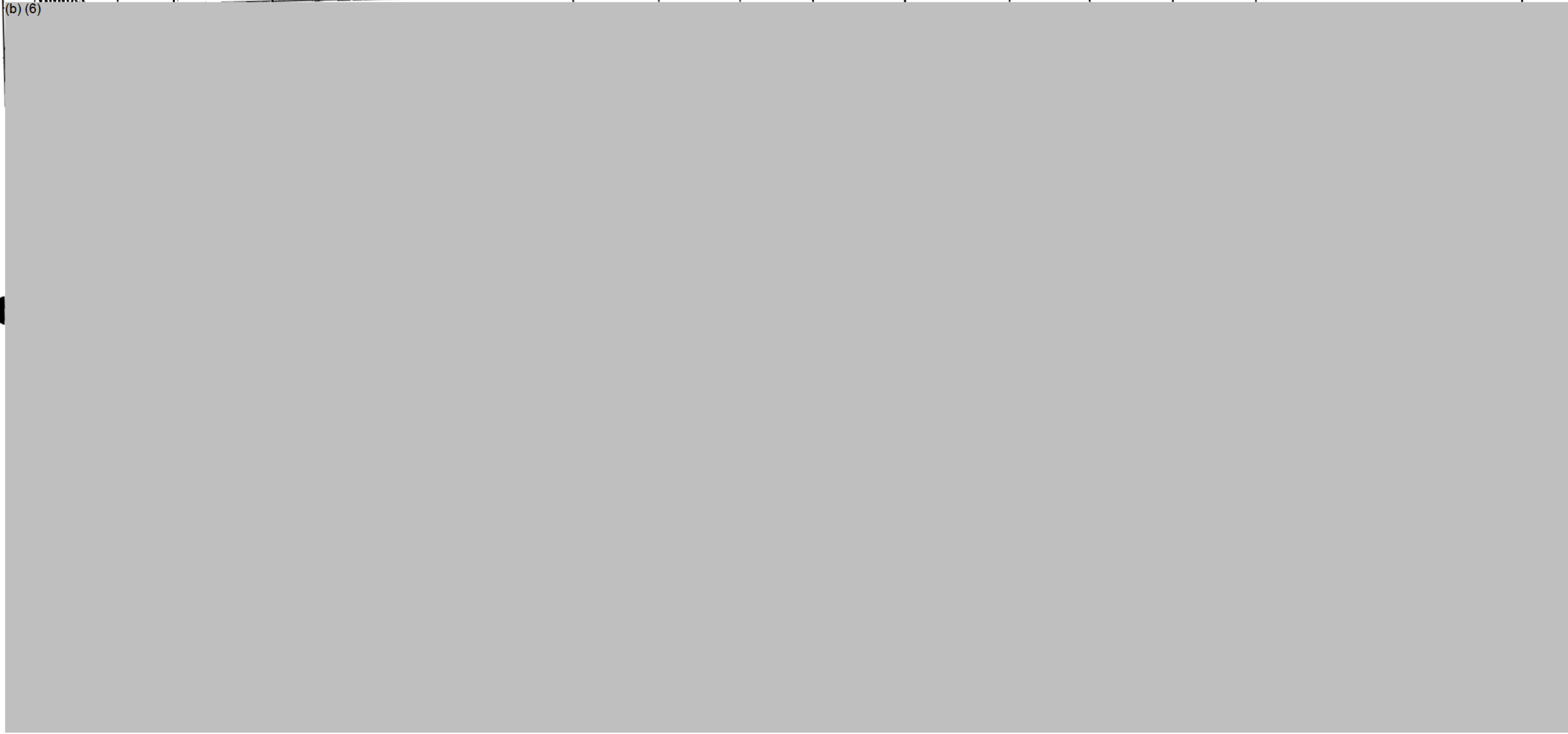
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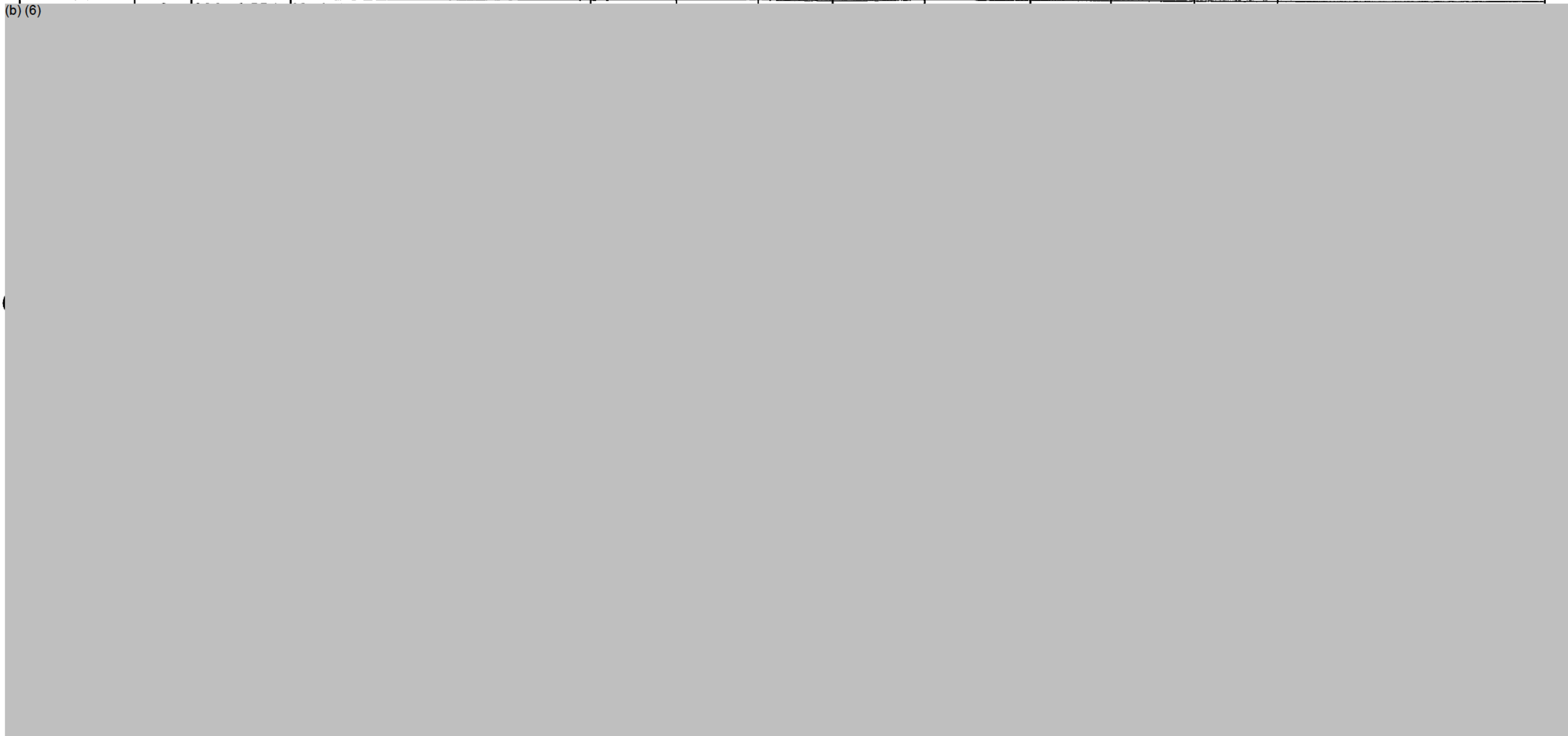
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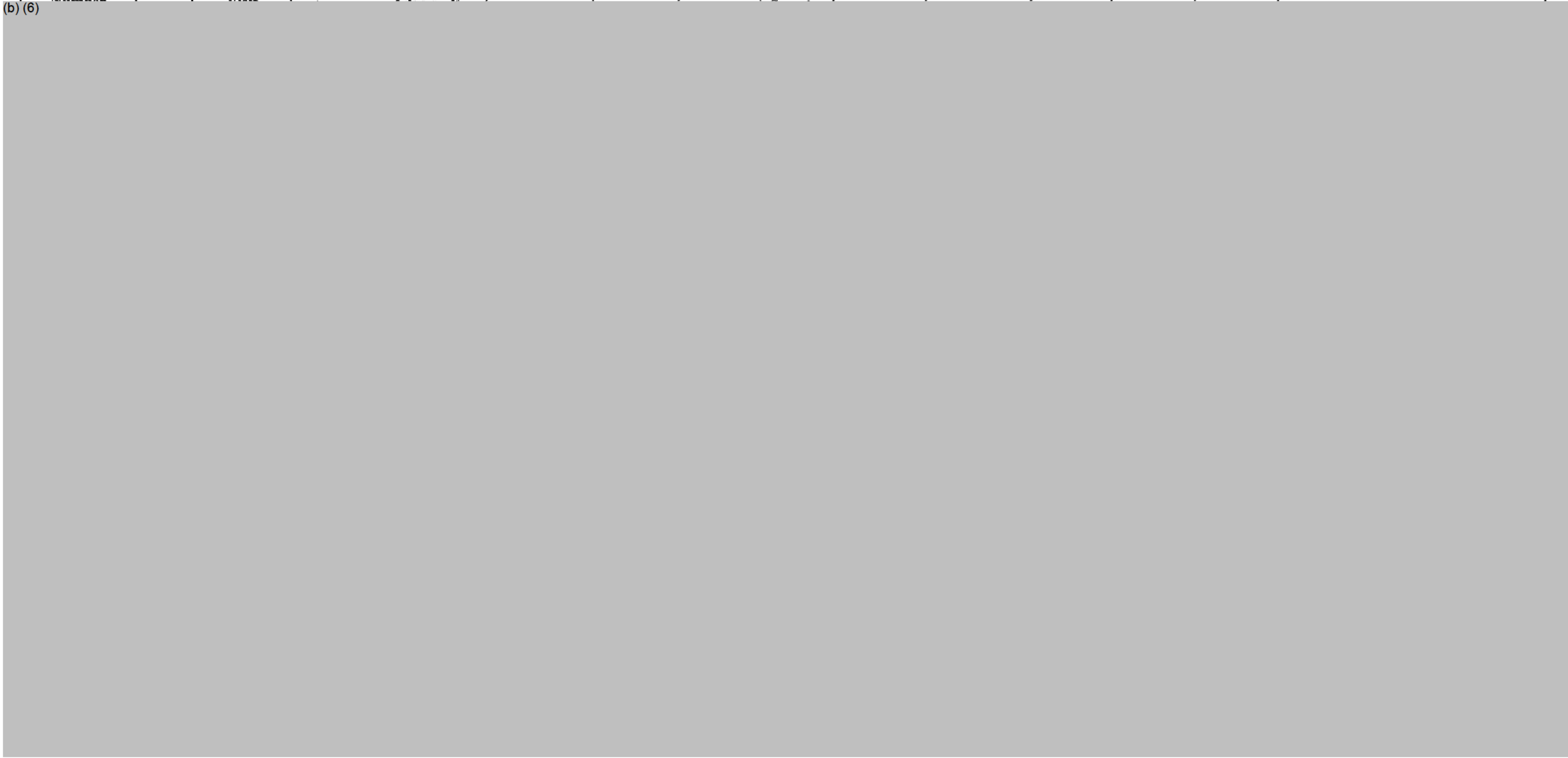


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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved		Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	
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Subject	Subject Event			Date of Onset	Date Resolved		Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	
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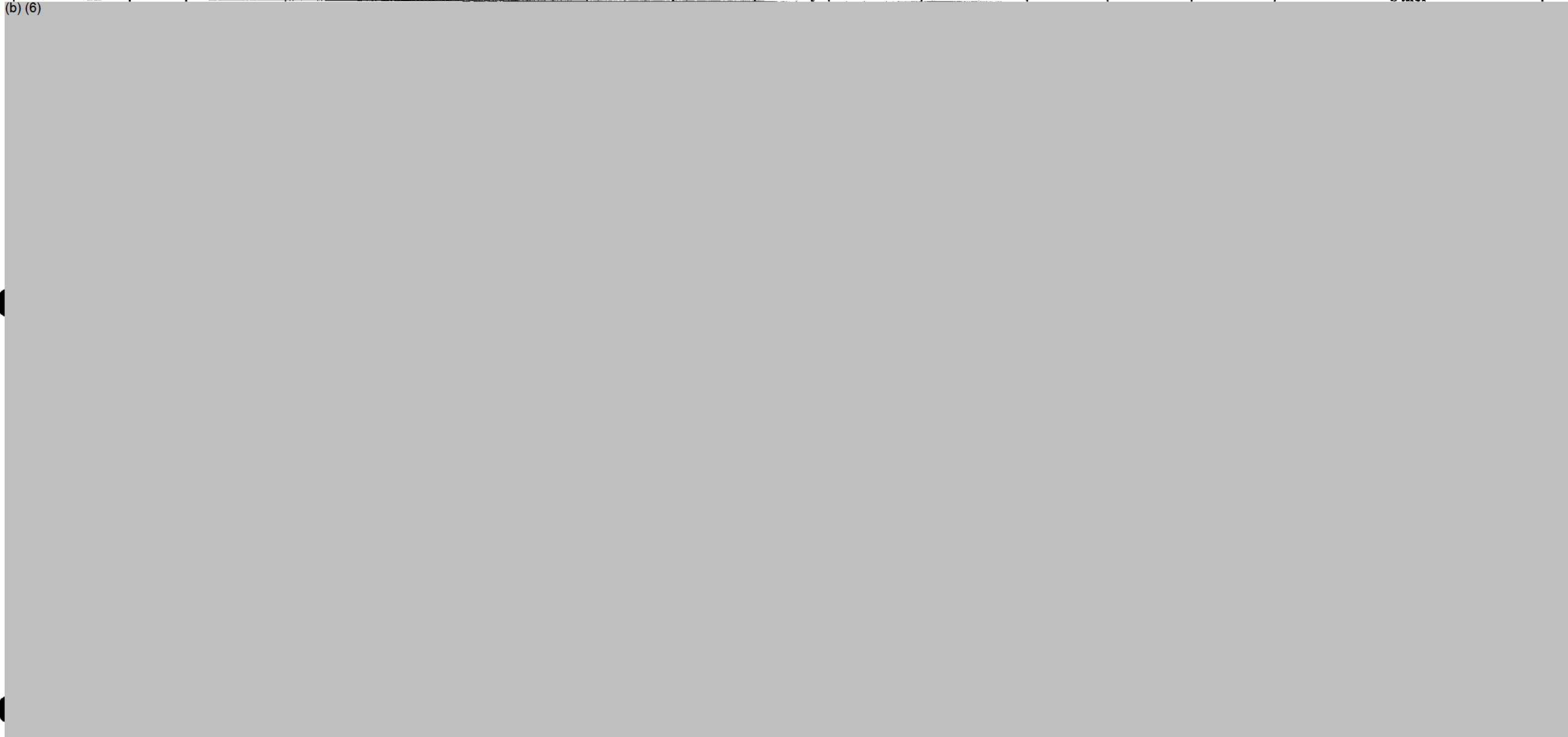
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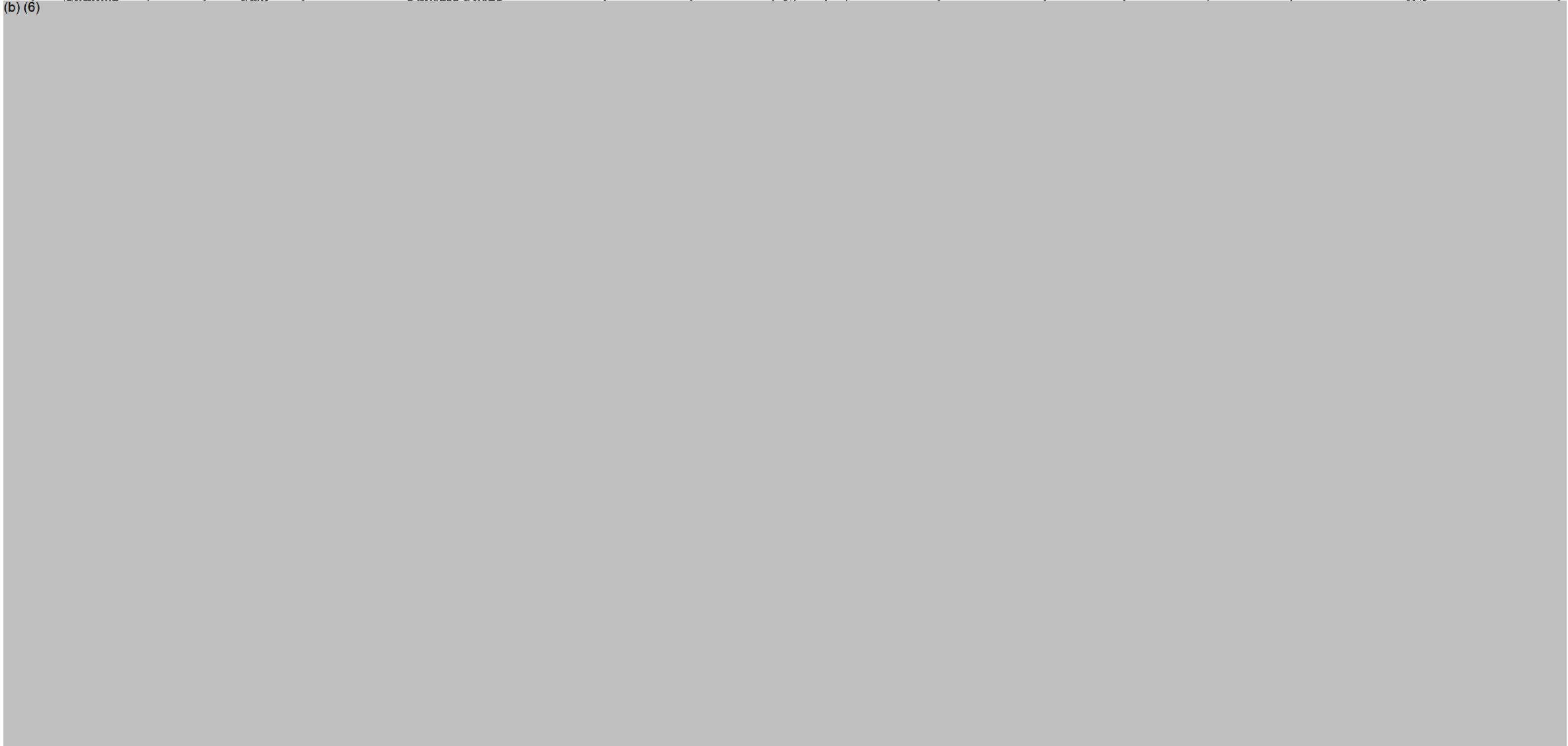


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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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Subject Event	Subject		Date of Onset	Date Resolved		Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	
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(b) (6)



Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	CA
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Subject Event Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Status	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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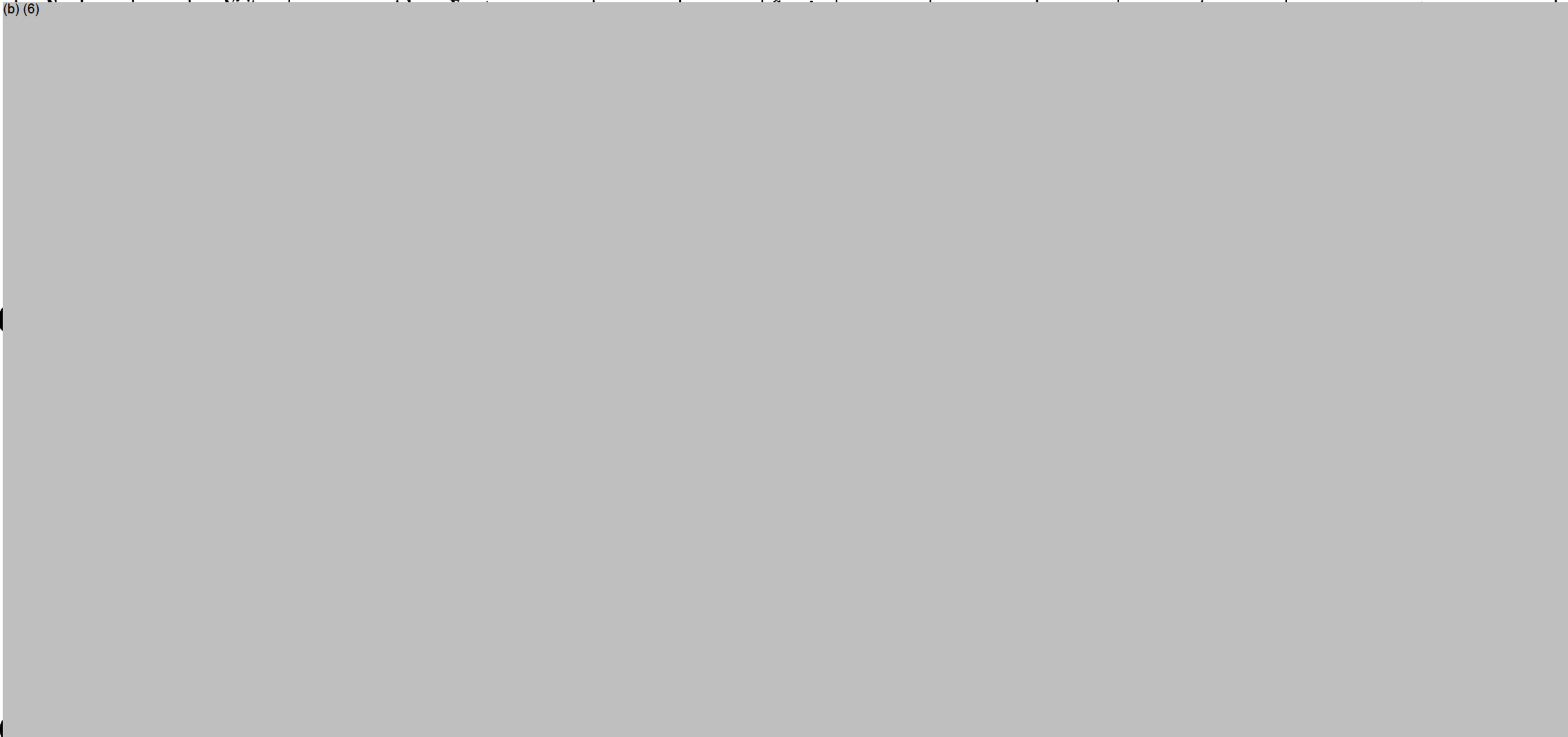
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40

Subject	Subject Event			Date of Onset	Date Resolved		Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	
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(b) (6)

41

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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42

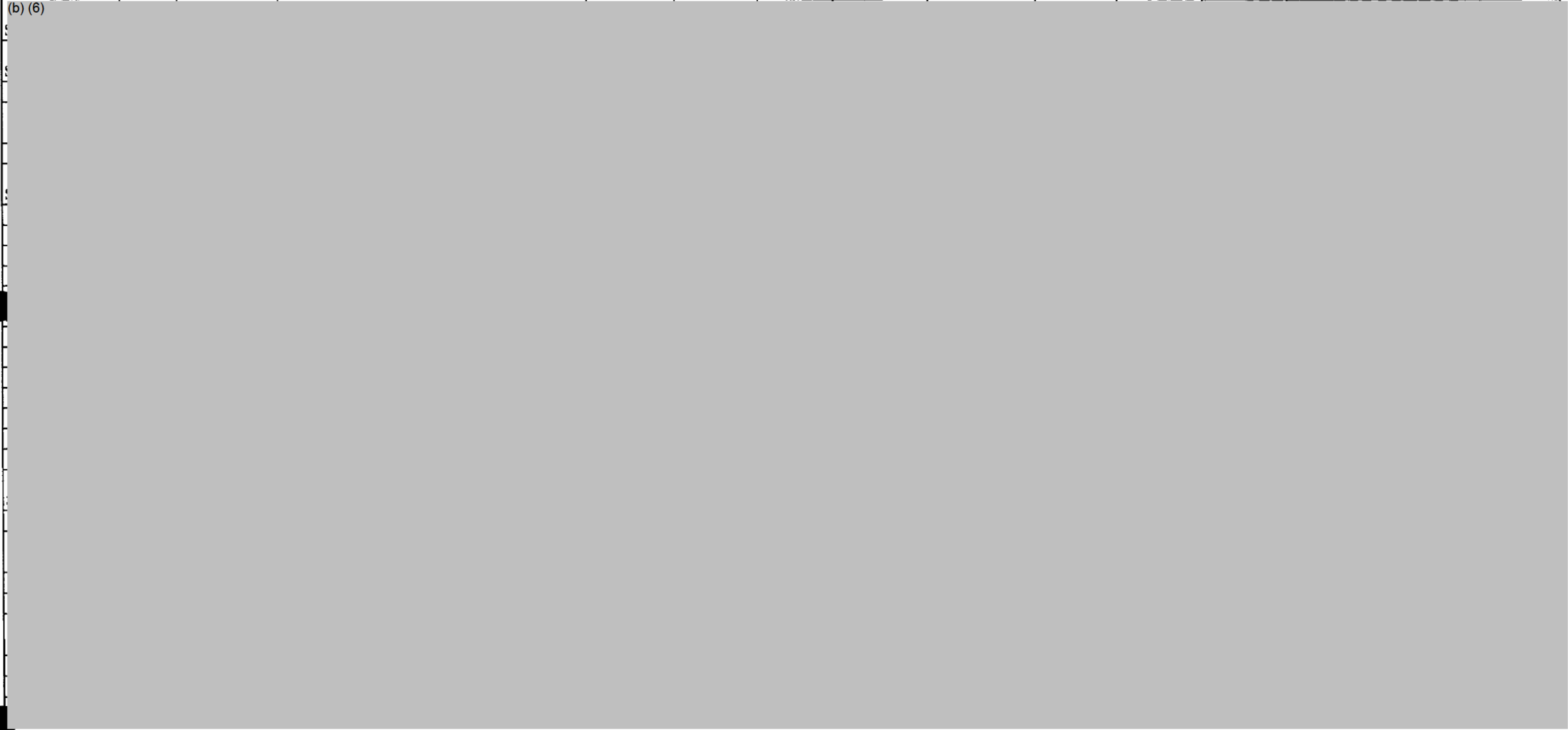
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(b) (6)



Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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44

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b) (6)



45

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b) (6)



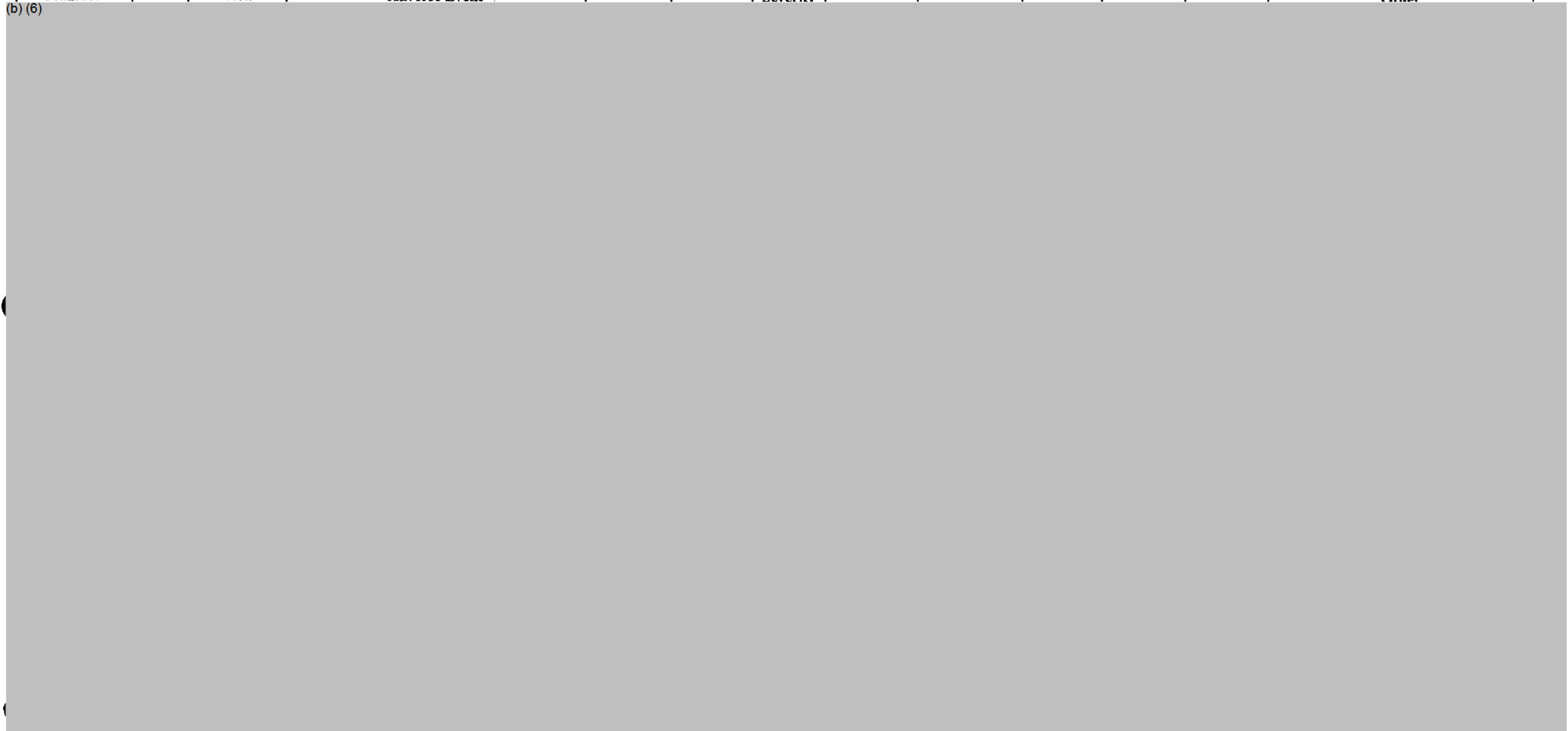
Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b) (6)



Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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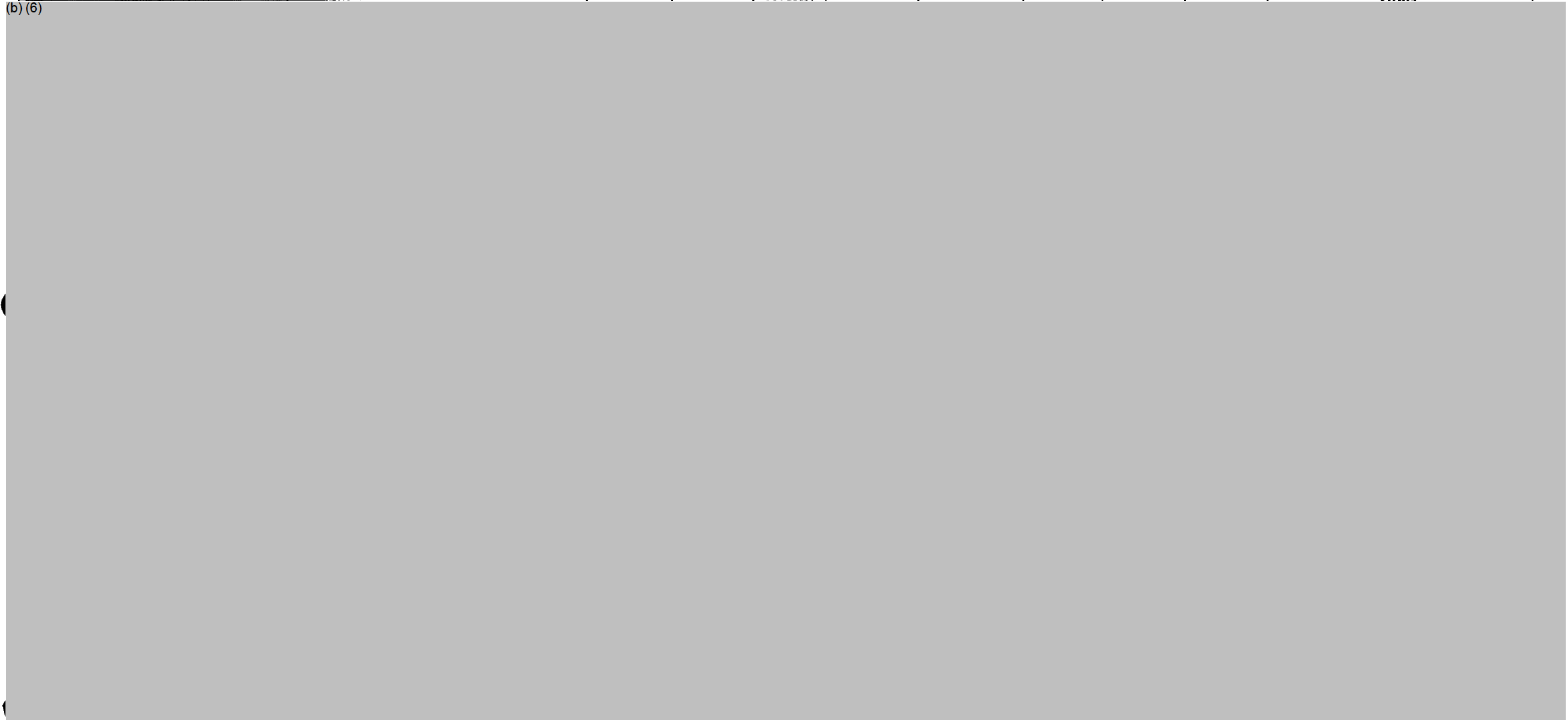
(b) (6)



48

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b) (6)



Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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STOP 2000

Subjects who Answered Yes to Experiencing Adverse Event at Some Point

But Did not Have an Adverse Event Record

Subject Number
(b)(6)

STOP 2000

Subjects who Had an Adverse Event Record

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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But Did not Answer Yes to Experiencing Adverse Event at Some Point

Subject Number
(b)(6)

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b)(6)

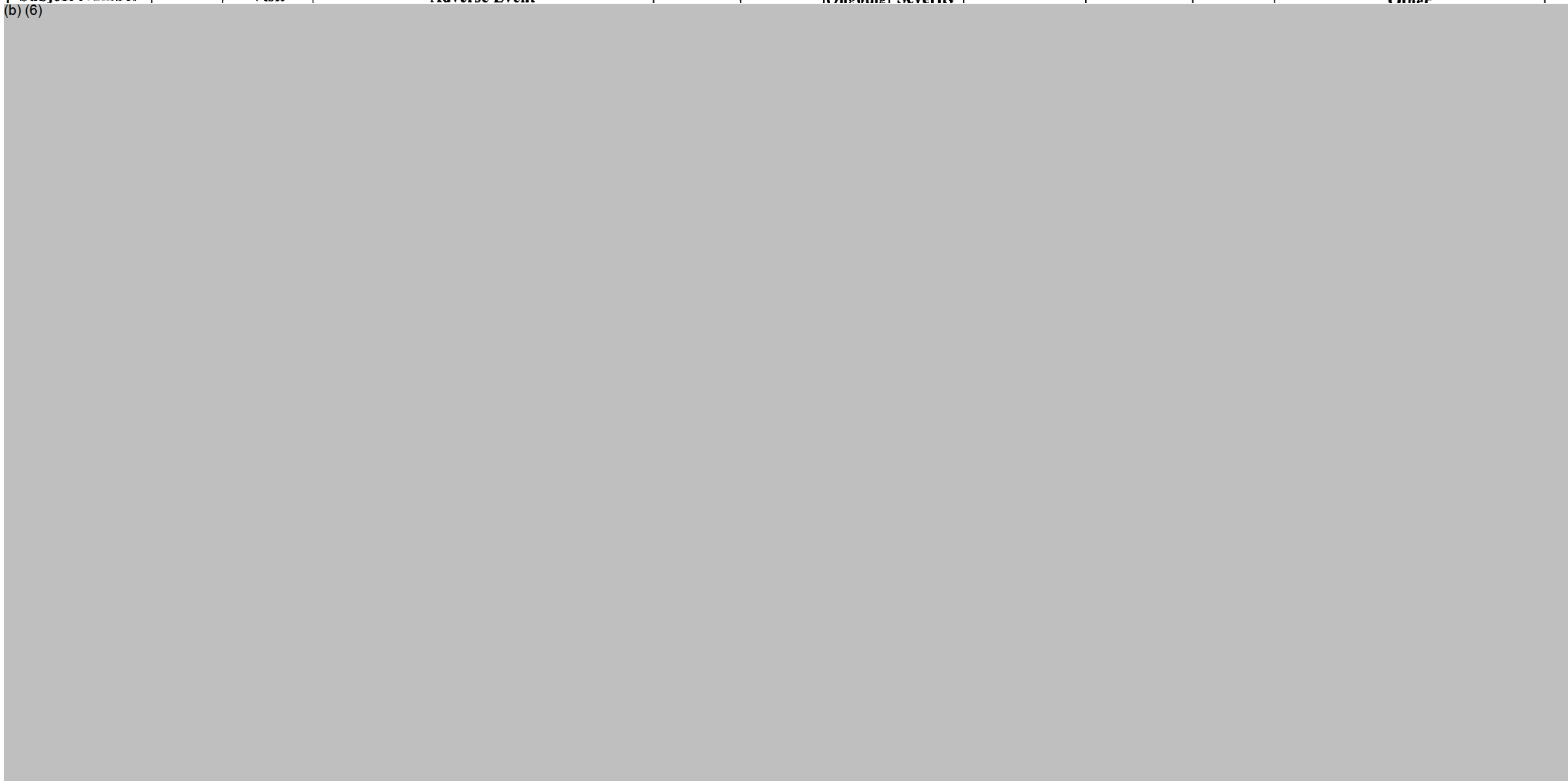
Subject Event Subject Number	Visit	Adverse Event	Date of Onset	Date Resolved	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Recovered Without Treatment	Recovered With Treatment	Other
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(b)(6)



Adverse Events From 12-24 month

Subject Number	Subject Event	Visit	Adverse Event	Date of Onset	Date Resolved	Ongoing	Severity	Relationship to Study Device	Event Unanticipated	Treatment Required	Other
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(b) (6)



(b) (6)



The SAS System

*Subjects who Had
an Adverse Event
Record*

*But Did not
Answer Yes to
Experiencing
Adverse Event at
Some Point*

Subject Number

(b)(6)



P020014/A18/CL/INR
PMA Amendment
Conceptus, Inc.

Conceptus Essure™ System

Amendment to PMA No. P020014

Table of Contents

Volume 11-
NOT RECOPIED FOR THIS AMENDMENT. PLEASE REFER TO
VOLUME 11 OF JUNE 5, 2002 PMA AMENDMENT FOR THE
BELOW DOCUMENTS

References for Pivotal Trial Report

RECEIVED
2002 OCT 16 A 10 09
FDA/CDRH/OCE/PMO

LDC

PMA AMENDMENT ROUTE SLIP

PMA NUMBER P020014/A019 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.

SHORT NAME CONCEPTUS

CONTACT (b)(6)

DIVISION _____

ADDRESS 1021 HOWARD AVE.

SAN CARLOS, CA 94070

PHONE NO. (b)(6)

FAX NO. (650) 610-8363

MANUFACTURER CONCEPTUS, INC.

REG NO. 2951250

(b)(4)

(b)(4)

***** REVIEW TIME SUMMARY *****

DATE ON SUBMISSION 17-OCT-2002

CYCLE # 1

DATE RECEIVED IN ODE 18-OCT-2002

CYCLE START 22-APR-2002

DATE FILING DUE _____

ELAPSED

LAST CYCLE

DATE DECISION DUE _____

FDA TIME

163

163

MFR TIME

16

16

AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
C001	<u>FILE</u>	<u>22-APR-2002</u>	
A001	<u>UMIN</u>	<u>03-MAY-2002</u>	
A002	<u>UMIN</u>	<u>16-MAY-2002</u>	
A003	<u>UMIN</u>	<u>28-MAY-2002</u>	
A004	<u>UMIN</u>	<u>07-JUN-2002</u>	
A005	<u>UMIN</u>	<u>13-JUN-2002</u>	
A006	<u>UMIN</u>	<u>24-JUN-2002</u>	
A007	<u>UMIN</u>	<u>24-JUN-2002</u>	
A008	<u>UMIN</u>	<u>18-JUL-2002</u>	
A009	<u>UMIN</u>	<u>21-AUG-2002</u>	
A010	<u>UMIN</u>	<u>21-AUG-2002</u>	
A011	<u>UMIN</u>	<u>23-AUG-2002</u>	
A012	<u>UMIN</u>	<u>04-SEP-2002</u>	
A013	<u>UMIN</u>	<u>16-SEP-2002</u>	
A014	<u>UMIN</u>	<u>23-SEP-2002</u>	
A015	<u>UMIN</u>	<u>23-SEP-2002</u>	

PMA AMENDMENT ROUTE SLIP

A016	<u>UMIN</u>	<u>27-SEP-2002</u>	
A017	<u>UMIN</u>	<u>30-SEP-2002</u>	
C002	<u>ADEF</u>	<u>30-SEP-2002</u>	<u>16-OCT-2002</u>
A018	<u>ADEF</u>	<u>16-OCT-2002</u>	

DRAERD REVIEWER RECORD FOR ORIGINAL 510(K)'S,
AND PMA AND IDE SUPPLEMENTS

Document No. _____ Reviewer _____ Date Assigned _____

CONSULTING REVIEWS DESIGNATED, AS APPROPRIATE, BY BRANCH CHIEF AND LEAD REVIEWER, AT THE BEGINNING OF THE REVIEW:

<u>SPECIALTY</u>	<u>REVIEW NEEDED?</u>		<u>REVIEWER</u>	<u>DATES</u>	
	YES	NO		SENT	RETURNED
CLINICAL	_____	_____	_____	_____	_____
ENGINEERING/ PHYSICS	_____	_____	_____	_____	_____
CHEMISTRY/ BIOMATERIALS	_____	_____	_____	_____	_____
SOFTWARE	_____	_____	_____	_____	_____
IMMUNOLOGICAL/ STERILITY	_____	_____	_____	_____	_____
TOXICOLOGY/ BIOCOMPATIBILITY	_____	_____	_____	_____	_____
STATISTICS	_____	_____	_____	_____	_____
OTHER _____	_____	_____	_____	_____	_____

COMMENTS:

REVISED 11/2/96 LMS
ON LAN AS REVREC.FRM

QUALITY CONTROL OVERVIEW OF DOCUMENT

A. ASSOC. DIRECTOR QC OVERVIEW: MEDICAL QC OF SUBMISSION IS NECESSARY?

YES _____ NO _____ INITIALS/DATE _____

B. IF YES IS NOTED ABOVE, MEDICAL OFFICER QC OVERVIEW:

1. Examination of the specialty reviews indicate there are remaining clinical issues that should be addressed (See attached sheet for summary).

INITIALS/DATE _____

2. In my opinion, all pertinent clinical issues have been adequately addressed.

FINAL SIGNOFF: MEDICAL OFFICER/DATE _____

FINAL SIGNOFF: ASSOC. DIRECTOR/DATE _____

REVISED: 1/2/96 LMS
LOCATED ON LAN AS REVREC.FRM

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

October 18, 2002

(b)(6)
CONCEPTUS, INC.
1021 HOWARD AVE.
SAN CARLOS, CA 94070

Dear (b)(6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) acknowledges receipt of your PMA AMENDMENT. This PMA AMENDMENT has been assigned the following unique document control number. Failure to reference this assigned number in future correspondence may result in processing delays.

PMA Number: P020014/A019
Dated: 17-OCT-2002
Received: 18-OCT-2002
Device: ESSURE SYSTEM

Any questions concerning this submission should be directed to the undersigned at (b)(6). All future correspondence regarding this PMA should be identified with the PMA number assigned above and should be submitted with the required number of copies to:

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

(b)(6)

Center for Devices and
Radiological Health

P020014/A19 ✓

Conceptus®

October 17, 2002

(b)(6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RECEIVED
2002 OCT 18 P 2:11
FDA/CDRH/ODE/PMO

RE: Amendment to PMA No. P020014
Post-Approval Study Protocols
Conceptus Essure™ System for Permanent Birth Control

Dear (b)(6):

This PMA Amendment is to provide the final protocols, statistical analysis plans, and case report forms for the two post-approval studies of the Essure System.

Exhibit A provides the protocol, statistical analysis plan, and case report forms for the post-approval study of the 5-year follow-up of the Phase II and Pivotal trial participants.

Exhibit B provides the protocol, statistical analysis plan, and case report forms for the post-approval study of placement rates among newly trained physicians in the commercial setting.

Please let me know if you have any questions regarding this PMA Amendment. I can be reached at (b)(6), or by fax at (b)(6) or by e-mail at (b)(6). Thank you for your continued review of this PMA application.

Sincerely,

(b)(6)

Attachments: Exhibit A and B

**Post-Approval Study of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials
(IDEs: G980152 and G000055)**

**Conceptus Research Protocol
Essure 5-Year**

**Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070
U.S.A.**

Telephone: (b) (6)

Fax: (650) 610-8363

REVISION HISTORY

Original Protocol, Rev 00

10/17/02

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Appendix A: Statistical Analysis Plan

Appendix B: Case Report Forms

- Pivotal Trial
- Phase II Study
- Histology

1. TITLE

“Post-approval study of the Essure System: 5 Year Follow-up under Phase II and Pivotal Trials.”

2. PURPOSE OF STUDY

The purpose of this study is to demonstrate the long-term safety and effectiveness of Essure in providing permanent contraception.

3. STUDY DESIGN

This protocol combines the long-term follow-up already planned under the Phase II (Conceptus protocols #STOP 07/10; IDE #G980152) and Pivotal trials (Conceptus protocol #STOP 2000; IDE #G000055). Specifically, study participants implanted with at least one Essure Micro-insert will be followed annually for 5 years.

Findings from the U.S. Collaborative Review of Sterilization (CREST¹ study) will be used as a qualitative assessment.

Reference

1. Peterson HB, Xia Z, Hughes JM, et al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-1170

4. STUDY PLAN

Study participants who received implantation with at least one Essure Micro-insert in the Phase II or Pivotal trials of the Essure System (gamma design) will be followed for 5 years. Participants who are not relying on Essure for contraception will be followed for safety evaluation only, at 2, 3, 4, and 5 years after implantation. Participants who are relying on Essure for contraception will be followed for safety and effectiveness evaluation at 2, 3, 4, and 5 years after discontinuation of alternative contraception. The Pivotal trial and Phase II protocols also include an 18 month follow-up visit for study participants who are relying on Essure for contraception. However, since this post-approval study protocol is intended to provide *annual* effectiveness rate information, the 18-month visit will not be included in this protocol. The data from the 18-month visit will instead be reported in the IDE annual progress reports. Participants terminated from the Phase II or Pivotal trial due to lack of Micro-insert placement,

Micro-insert explantation, or who have become lost-to-follow-up in those studies, will not be followed under this protocol.

5. PRIMARY AND SECONDARY ENDPOINTS

5.1 The primary endpoints for the study are as follows:

1. Prevention of pregnancy for 5 years,
2. Safety of device wearing for 5 years

Pregnancy prevention will be determined by a pregnancy test at the 2 and 5 year follow-up visits and by phone assessment at the 3 and 4 year follow-up visits. Safety of device wearing will be evaluated by recording adverse events at each of the scheduled follow-up visits.

5.2 The secondary endpoint for the study are as follows:

1. Participant satisfaction with device wearing for 5 years,

Participant satisfaction with device wearing will be evaluated by participant interviews at scheduled follow-up visits.

6. INVESTIGATORS AND QUALIFICATIONS

The Investigators who participated in the Phase II and Pivotal trials will be the same Investigators who participate under this post-approval study protocol.

7. STUDY POPULATION

Study participants will be women who received implantation of at least one Essure Micro-insert in the Pivotal trial and participants in the Phase II trial that received at least one Micro-insert and agreed to be followed for 5 years¹.

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This study will not include those women terminated from the Phase II or Pivotal trials.

8. STUDY PROCEDURES

The case report forms for this study are included in **Appendix B**. These case reports forms are the same as currently used in the Phase II and Pivotal trials, with the addition of the case report forms that will be used for histology results (which are the same as those used in the pre-hysterectomy study of Essure; G960206).

All study procedures will be paid for by the Sponsor.

9.1 Follow-up Visits and Phone Contact

A description of each visit and phone contact is provided below.

- 9.1.1 Phone contact will be scheduled at three and four years following discontinuation of alternative contraception.
- 9.1.2 Office visits will be scheduled two and five years following discontinuation of alternative contraception.
- 9.1.3 Any participant who has had one or more Essure devices implanted, but is not able to rely on the device(s) for contraception, for any reason, will be followed at the 2, 3, 4 and 5 year follow-up time points (post-device placement) for safety and participant tolerance to device wearing. This includes participants who have had incisional sterilization, subsequent to Essure Micro-insert placement but without Micro-insert removal.
- 9.1.4 Additional office visits required for the investigation or management of an adverse event(s) must be recorded on the "Unscheduled Visit" Case Report Form.

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9.4 Intrauterine Procedures Post-Essure Placement

Participants will be instructed to contact the Investigator if they are scheduled to undergo any intrauterine procedure such as endometrial biopsy, dilatation and curettage (D&C), or hysteroscopy (diagnostic or operative) including endometrial ablation or resection. If such a procedure(s) is scheduled, the Investigator should inform the physician who will be conducting the procedure that there may be risks associated with the presence of the Essure Micro-inserts that, at this time, have not been identified. In the event of a hysteroscopic procedure, the Investigator will request the physician to make an evaluation of the tissue surrounding any portion of the Essure Micro-insert trailing into the uterine cavity and to provide photos and video footage when possible.

9.5 Extirpative Surgery of Reproductive Organs Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any extirpative surgery of the reproductive organs (hysterectomy, salpingectomy, oophorectomy), *for any reason*, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes and provide photos and video footage when possible. In the event that the extirpative surgery occurs in a participant whose devices were known to be located in her peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the

location of the device, a determination as to whether the device(s) were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s). The search for the device should be limited to 30 minutes, and any free-floating devices should be retrieved and returned to Conceptus. The Investigator should obtain the excised fallopian tubes, when possible, and send them to Conceptus for histological evaluation. In any case, histology specimens retrieved should be evaluated and results forwarded to the Investigator and Conceptus. When the tubes are sent to Conceptus for evaluation, the case report forms attached as Appendix B will be used. If the participant is scheduled to undergo any intrauterine sampling procedure (D&C, endometrial biopsy), histology results should also be forwarded to the Investigator and Conceptus.

9.6 Transabdominal Surgery Post-Essure Placement

Participants who have had Essure Micro-insert(s) implanted and are subsequently scheduled to undergo any surgery in the peritoneal cavity that would permit visualization and evaluation of the fallopian tube exterior, will be instructed to contact the Investigator. The Investigator will request the operating surgeon to make an evaluation of the exterior of the fallopian tubes, and provide photos and video footage when possible. In the event that the surgery occurs in a patient whose devices were known to be located in the peritoneal cavity but were not previously retrieved, the Investigator will request the operating surgeon to perform a search for the device(s), and if located, provide a description of the location of the device, a determination as to whether the devices were free-floating or adherent, and an evaluation of the condition of the tissue surrounding the device(s).

10 ADVERSE EVENTS

Adverse events are defined as any untoward deviations in subject health away from baseline. Investigators must record and document all adverse events in the case report form, and record and report any unanticipated device related adverse effects to Conceptus and the reviewing IRB / Ethics Committee as soon as possible but no longer than 5 working days after becoming aware of the event. Unanticipated adverse device effect means any serious adverse effect on health or safety, or any life-threatening problem or death caused by or associated with a device, *if* that effect, problem or death was not previously identified in nature,

severity or degree of incidence in the investigational plan *or* any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. For all serious adverse events, the Investigator will send to Conceptus all appropriate paperwork (discharge summaries, office notes, etc.) that might be pertinent.

11 RECORDS AND REPORTS

11.1 Each Investigator will maintain the following accurate, complete and current records relating to the Investigator's participation in an investigation:

(b) (4)



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(b) (4)



(b) (4)



(b) (4)



15. DATE OF COMMENCEMENT

The proposed date of commencement for this post-approval study plan is immediately upon PMA approval.

Appendix A
STATISTICAL ANALYSIS PLAN

Post-approval study of the Essure System
5-Year Follow-up
under Phase II (STOP 07/10) and Pivotal (STOP 2000) Trials

(IDEs: G980152 and G000055)

Conceptus Research Protocol
Essure 5-Year

Statistical Plan Summary

(b) (4)



Bayesian Perspective

(b) (4)



³ <http://www.mrc-bsu.cam.ac.uk/bugs/welcome.shtml>

Appendix B

CASE REPORT FORMS

- 1. Pivotal Trial (STOP 2000)**
- 2. Phase II Study (STOP 07/10)**
- 3. Histology**

Essure™ System
US Post-Approval Study for Newly Trained Physicians

October 17, 2002

Conceptus Protocol:
Essure PAS Placement

Sponsor:

Conceptus Incorporated
1021 Howard Avenue
San Carlos, CA 94070

Telephone 650-628-4700

Fax 650-802-2890

REVISION HISTORY

Version 01

October 17, 2002

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6. Inclusion and Exclusion Criteria
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8. Instructions for Use
9. Records and Reports
10. Statistical Analysis and Reporting of Results
11. Financial Issues
12. Study period

Appendices

- A. Case Report Forms**
- B. Statistical Analysis Plan**

1. Title

The title of this study is “Essure™ System US Post-Approval Study for Newly Trained Physicians”.

2. Study Purpose

The purpose of the Plan is to assess the bilateral placement rate in the commercial setting in newly trained physicians. The purpose is also to gather additional data regarding placement failure, to determine if there are any common characteristics that can be useful in future patient selection.

3. Study Design

This study is designed to collect demographic and micro-insert placement data on a total of 800 women from 40 physicians in the commercial setting in whom an Essure System is placed through the operating channel of the hysteroscope. Data will also be collected on women in whom the procedure is begun, but in whom an Essure System is not placed through the operating channel of the hysteroscope (“non-attempts”), but this is in addition to the 800 women in whom there is an attempt at placement with Essure.

Although only 40 physicians are needed to reach a total of 800 women, 45 physicians will be enrolled in this study in the event that not all physicians complete a total of 20 cases, or do so on a timely basis. Enrollment in this study will cease after data is available from 40 physicians who have provided data regarding 20 cases of Essure placement attempt.

Physician enrollment in this study will be limited to no more than 6 physicians from any one state, and no more than 2 physicians from any one institution. In

addition, no more than two-thirds of the physicians will represent either community-based hospitals or teaching institutions.

The first 45 physicians in major metropolitan areas in the United States who complete the didactic and model portions of the training program will be asked to participate in this study. Such physicians will be enrolled in the study only if: 1) they agree to participate, and 2) they do not have previous experience in Essure micro-insert placement. In addition, they will not contribute cases to this study until after they have completed the preceptoring portion of the training program.

The enrolled physicians will then collect demographic and micro-insert placement data on the first cases performed after preceptoring is complete, until placement data are available on a total of 20 women in whom an Essure System was placed through the operating channel of the hysteroscope. Since data on “non-attempts” will also be collected, it is anticipated that more than 800 women will be enrolled in order to obtain data on 800 women with an actual placement attempt.

Physicians enrolled in this study will include the following statement in their informed consent of the patient:

“I agree to participate in the Postmarket Surveillance Study being conducted on the Essure System. I acknowledge that there is no benefit to me for participating in this study. I agree to allow information about me and my placement procedure to be shared with the Sponsor, Conceptus, its employees and consultants, and the FDA. I understand that the information sent to the Sponsor and the FDA will not identify me, but that Conceptus or the FDA may have reasons to review identifiable information about me in the office of my physician.”

4. **Primary Endpoints**

The primary endpoints are as follows:

1. Bilateral micro-insert placement rate, and
2. Identification of factors predictive of micro-insert placement failure

Some women may not achieve bilateral placement until after two micro-insert placement procedures. This study will only incorporate placement data from the 1st micro-insert placement procedure for each patient. So, if a patient receives unilateral placement during the first placement procedure and an Essure micro-insert is successfully placed in the contralateral tube during the second placement procedure, then the placement status for such a patient under this study would be “unilateral placement”, even though bilateral placement was eventually achieved.

Bilateral micro-insert placement success or failure will be noted on the Case Report Forms (CRFs) for the first placement procedure for a given patient. The following demographic information will also be collected on the CRFs to determine if any of these variables are predictive factors for placement failure:

- race
- age
- education level
- weight
- height
- income
- gravidity
- parity
- number of vaginal births
- number of abortions
- history of PID/salpingitis
- history of prior abdominal/pelvic surgery

- unusual uterine anatomy (unicornuate uterus, bifurcated uterus)
- other remarkable obstetric or gynecological history
- body mass index
- contraceptive method used just prior to Essure placement procedure
- time in menstrual cycle when Essure placement procedure was performed
- whether the patient received hormonal manipulation to promote atrophic or proliferative endometrium prior to placement procedure

In addition, the level of prior hysteroscopic experience of the physician and certain procedure details (equipment, distension, anesthesia method, etc.) will be recorded.

5. Designated Person

The Director of Professional Education at Conceptus will be responsible for execution of this study, and the V.P. of Clinical Research and Medical Affairs will be responsible for the data analysis and report preparation.

6. Inclusion and Exclusion Criteria

All inclusion and exclusion criteria from the Instructions for Use approved under the PMA will apply.

Additional inclusion criteria:

- Women who are willing to allow their data to be shared with the Sponsor and the FDA.

7. Data collection

Data will be collected using standardized Case Report Forms (CRFs). The Physician or his/her designee will enter the relevant information into electronic case report forms. The questions to be incorporated into the electronic CRFs for this study are attached as **Appendix A**.

No patient follow-up will be conducted as part of this study, with the exception of data from follow-up HSGs performed to evaluate the reasons for placement failure in women who desire a second attempt at device placement (although, as stated above, the data from the second attempt will not be recorded under this protocol).

8. Instructions for Use

Micro-insert placement will be performed according to the Instructions for Use (IFU) approved under the Essure PMA (P020014).

9. Records and Reports

Records

The following records will be maintained by Conceptus during the course of this study, and for two years after acceptance of the final study report by the FDA:

- All correspondence with the physicians or FDA regarding this study, including required reports,
- Signed agreements from each of the Physicians, stating the commitment to conduct the study in accordance with the approved protocol,
- The approved protocol, with documentation of the date and reason for any deviation from the protocol, and
- All data collected and analyses conducted in support of the study.

The following records will be maintained by the Physician during the course of the study, and for two years after acceptance of the final study report by the FDA:

- All correspondence between physicians, FDA, and Conceptus regarding this study and any data collected as part of the study
- The approved protocol, with documentation of the date and reason for any deviation from the protocol
- All data collected under this study

Content and timing of reports

A final report will be submitted to FDA within 3 months of receipt of data regarding the 800th patient to undergo an Essure placement procedure under this study. It is anticipated that patient enrollment will be completed in approximately one year from study commencement. If enrollment takes longer than planned, an interim report will be submitted one year from the date of commencement of the study, to be followed with a final report on all patients.

The report(s) will include the information relating to the bilateral placement rates of newly trained commercial physicians as well as an analysis of factors that may impact bilateral placement (see Section 4 above for a list of these potential factors).

10. Statistical Analysis and Reporting of Results

The Statistical Analysis Plan is attached as **Appendix B**.

11. Financial Issues

(b) (4)



(b) (4)



12. Study period

The study is anticipated to commence within 2 months of PMA approval, and is expected to be approximately 12 months in duration.

Appendix A

Case Report Forms

P020014/A²⁰:c1

Conceptus.

October 18, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: Amendment to PMA No. P020014
Expiration Dating
Conceptus Essure™ System for Permanent Birth Control

RECEIVED
2002 OCT 21 A 10:48
FDA/CDRH/OCE/PMO

Dear (b) (6):

Pursuant to our teleconference of October 8, 2002, we are submitting this PMA Amendment for the following reasons:

(b) (4), (b) (6)

[Redacted content]

Sincerely,

(b) (6)

[Redacted signature]

PMA Amendment, 10.18.02
Expiration Dating

Page 1 of 1

SP 15

P020014/A²¹; C1, V1

Conceptus.

October 18, 2002

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

RECEIVED

OCT 21 11 44 AM '02

FDA/CDRH/OCE/DIC

Re: P020014
Essure System for Permanent Birth Control
Letter of Agreement and Response to Approvable Letter

To Whom It May Concern:

We have received your Approvable Letter dated September 30, 2002, and we concur with the "Conditions of Approval" which were enclosed with the Approvable Letter and all other restrictions as stated in the Approvable Letter.

(b) (4)



P020014
Essure System
Letter of Agreement
October 18, 2002

Page 1 of 2

(b) (4)



We do not have any additional information provided in this response that is not identified above.

If you have any questions, I can be reached at (b) (6), or by fax at (b) (6) - (b) (6) or by e-mail at (b) (6). Thank you.

Sincerely,

(b) (6)



P020014
Essure System
Letter of Agreement
October 18, 2002

Page 2 of 2

2

P020014/A22
C2

Conceptus.

October 21, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

FDA/CDRH/OCE/PMO
2002 OCT 22 P 12: 30
RECEIVED

Re: Amendment to PMA No. P020014
Expiration Dating, modified language in #2 below
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6)

Pursuant to our teleconference of October 8, 2002, we are submitting this PMA Amendment for the following reasons:

(b) (4)

Sincerely,

(b) (6)

PMA Amendment, 10.21.02
Expiration Dating

Page 1 of 1

SP
1

P020014 A23/C/V/

Conceptus.

November 5, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

FDA/CDRH/OCE/PMO
2002 NOV -6 A 10:53
RECEIVED

Re: Amendment to PMA No. P020014
Final labeling and training manual
Conceptus Essure™ System for Permanent Birth Control

Dear (b) (6) :

Enclosed are the final printed physician labeling, final printed patient labeling, and final printed training manual.

Physician Labeling (Volume I, Appendix A)

(b) (4)



SP9 1

Patient Labeling (Volume 1, Appendix B)

(b) (4)



If you have any questions, I can be reached at (b) (6), or by fax at (b) (6) or by e-mail at (b) (6). Thank you.

Sincerely,

(b) (6)



Enclosures: Volumes 1 and 2

P020014
VI
CL

Pre-Market Submission
Cover Sheet

CDRH SUBMISSION COVER SHEET				
Date of Submission: April 19, 2002			FDA Document Number: PMA Shell Number M010031	
Section A Type of Submission				
PMA	PMA Supplement	PDP	510(k)	Meeting
<input checked="" type="checkbox"/> Original submission <input type="checkbox"/> Modules submission <input type="checkbox"/> Amendment <input type="checkbox"/> Report <input type="checkbox"/> Report Amendment PMA & Expedited Review Request	<input type="checkbox"/> Regular <input type="checkbox"/> Special <input type="checkbox"/> Panel Track <input type="checkbox"/> 30-day Supplement <input type="checkbox"/> 30-day Notice <input type="checkbox"/> 135-day Supplement <input type="checkbox"/> Real-time Review <input type="checkbox"/> Amendment to PMA Supplement	<input type="checkbox"/> Presubmission summary <input type="checkbox"/> Original PDP <input type="checkbox"/> Notice of intent to start clinical trails <input type="checkbox"/> Intention to submit Notice of Completion <input type="checkbox"/> Notice of Completion <input type="checkbox"/> Amendment to PDP <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated <input type="checkbox"/> Additional information <input type="checkbox"/> Traditional <input type="checkbox"/> Special <input type="checkbox"/> Abbreviated	<input type="checkbox"/> Pre-IDE meeting <input type="checkbox"/> Pre-PMA meeting <input type="checkbox"/> Pre-PDP meeting <input type="checkbox"/> 180-day meeting <input type="checkbox"/> Other (specify):
IDE	Humanitarian Device Exemption	Class II Exemption	Evaluation of Automatic Class III Designation	Other Submission
<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement	<input type="checkbox"/> Original submission <input type="checkbox"/> Amendment <input type="checkbox"/> Supplement <input type="checkbox"/> Report	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	<input type="checkbox"/> Original submission <input type="checkbox"/> Additional information	Describe submission:
Section B Applicant or Sponsor				
Company / Institution name: Conceptus Incorporated		Establishment registration number: 2951250		
Division name (if applicable): Not Applicable		Phone number (include area code): (b) (6)		
Street address: 1021 Howard Avenue		FAX number (include area code): (b) (6)		
City: San Carlos	State/Province: CA 94070		Country: USA	
Contact name: (b) (6)				
Contact title: (b) (6)			Contact e-mail address: susan_aloyan@conceptus.com	
Section C Submission correspondent (if different from above)				
Company/Institution name: Same as above		Establishment registration number: Same as above		
Division name (if applicable): Same as above		Phone number (include area code): (b) (6)		
Street address: Same as above		FAX number (include area code): Same as above		
City: Same as above	State/Province: Same as above		Country: Same as above	
Contact name: Same as above				
Contact title: Same as above			Contact e-mail address: Same as above	

Section D1 Reason for Submission - PMA, PDP, or HDE		
<input checked="" type="checkbox"/> New device <input type="checkbox"/> Withdrawal <input type="checkbox"/> Additional or expanded indications <input type="checkbox"/> Licensing agreement	<input type="checkbox"/> Change in design, component, or specifications: <input type="checkbox"/> Software <input type="checkbox"/> Color Additive <input type="checkbox"/> Material <input type="checkbox"/> Specifications <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Location change: <input type="checkbox"/> Manufacturer <input type="checkbox"/> Sterilizer <input type="checkbox"/> Packager <input type="checkbox"/> Distributor
<input type="checkbox"/> Process Change: <input type="checkbox"/> Manufacturing <input type="checkbox"/> Sterilization <input type="checkbox"/> Packaging <input type="checkbox"/> Other (specify below)	<input type="checkbox"/> Labeling change: <input type="checkbox"/> Indications <input type="checkbox"/> Instructions <input type="checkbox"/> Performance characteristics <input type="checkbox"/> Shelf Life <input type="checkbox"/> Trade Name <input type="checkbox"/> Other (specify below)	Report submissions: <input type="checkbox"/> Annual or periodic <input type="checkbox"/> Post-approval study <input type="checkbox"/> Adverse reaction <input type="checkbox"/> Device defect <input type="checkbox"/> Amendment
<input type="checkbox"/> Response to FDA correspondence: <input type="checkbox"/> Request for applicant hold <input type="checkbox"/> Request for removal of applicant hold <input type="checkbox"/> Request for extension <input type="checkbox"/> Request to remove or add manufacturing site		<input type="checkbox"/> Change in ownership <input type="checkbox"/> Change in correspondent
<input type="checkbox"/> Other reason (specify):		
Section D2 Reason for Submission - IDE		
<input type="checkbox"/> New device <input type="checkbox"/> Addition of institution <input type="checkbox"/> Expansion/extension of study <input type="checkbox"/> IRB certification <input type="checkbox"/> Request hearing <input type="checkbox"/> Request waiver <input type="checkbox"/> Termination of Study <input type="checkbox"/> Withdrawal of application <input type="checkbox"/> Unanticipated adverse effect <input type="checkbox"/> Notification of emergency use <input type="checkbox"/> Compassionate use request <input type="checkbox"/> Treatment IDE <input type="checkbox"/> Continuing availability request	<input type="checkbox"/> Change in: <input type="checkbox"/> Correspondent <input type="checkbox"/> Design <input type="checkbox"/> Informed Consent <input type="checkbox"/> Manufacturer <input type="checkbox"/> Manufacturing process <input type="checkbox"/> Protocol - feasibility <input type="checkbox"/> Protocol - other <input type="checkbox"/> Sponsor <input type="checkbox"/> Report Submission: <input type="checkbox"/> Current investigator <input type="checkbox"/> Annual progress <input type="checkbox"/> Site waiver limit reached <input type="checkbox"/> Final	<input type="checkbox"/> Response to FDA letter concerning: <input type="checkbox"/> Conditional approval <input type="checkbox"/> Deemed approved <input type="checkbox"/> Deficient final report <input type="checkbox"/> Deficient progress report <input type="checkbox"/> Deficient investigator report <input type="checkbox"/> Disapproval <input type="checkbox"/> Request extension of time to respond to FDA <input type="checkbox"/> Request meeting
<input type="checkbox"/> Other reason (specify):		
Section D3 Reason for Submission - 510(k)		
<input type="checkbox"/> New device <input type="checkbox"/> Addition or expanded indications <input type="checkbox"/> other reason (specify):	<input type="checkbox"/> Change in technology <input type="checkbox"/> Change in design	<input type="checkbox"/> Change in materials <input type="checkbox"/> Change in manufacturing process

Section E Additional Information on 510(k) Submissions							
Product codes of devices to which substantial equivalence is claimed:				Summary of, or statement concerning, safety and effectiveness data:			
1	2	3	4	<input type="checkbox"/> 510 (k) summary attached <input type="checkbox"/> 510 (k) statement			
5	6	7	8				
Information on devices to which substantial equivalence is claimed:							
510(k) Number		Trade or proprietary or model name			Manufacturer		
1		1		1			
2		2		2			
3		3		3			
4		4		4			
5		5		5			
6		6		6			
Section F Product Information - Applicable to All Applications							
Common or usual or classification name: Device, Occlusion, Tubal, Contraceptive							
Trade or proprietary or model name				Model number			
1 Essure (formerly STOP Device) System				PCD 001/ ESS001			
2							
3							
4							
5							
FDA document numbers of all prior related submissions (regardless of outcome):							
1 G960052	2 G960206	3 G980152	4 G000055	5 G010223	6 I010191		
7 M010031/I	8 M010031/II	9 M010031/III	10 M010031/IV	11 010031/V	12		
Data included in submission : <input checked="" type="checkbox"/> Laboratory testing <input type="checkbox"/> Animal trials <input checked="" type="checkbox"/> Human trials							
Section G Product Classification - Applicable to All Applications							
Product code: KNH		C.F.R. section 884.5380		Device class: <input type="checkbox"/> Class I <input type="checkbox"/> Class II <input checked="" type="checkbox"/> Class III <input type="checkbox"/> Unclassified			
Classification panel: Obstetrics/Gynecology							
Indications (From labeling): The Essure™ System is indicated for permanent birth control (female sterilization) by occlusion of the fallopian tubes.							

[REDACTED]			FDA Document Number:		
Section H Manufacturing/ Packaging/ Sterilization Sites					
<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		FDA establishment registration number: 2951250		<input checked="" type="checkbox"/> Manufacturer <input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Contract manufacturer <input type="checkbox"/> Repackager/relabeler	
Company/institution name: Conceptus Incorporated			Establishment registration number: 2951250		
Division name (if applicable): Not Applicable			Phone number (include area code): (b) (6)		
Street address: 1021 Howard Avenue			Fax number (include area code): (b) (4)		
City: San Carlos		State/Province: CA		Country: USA	
ZIP/Postal Code: 94070					
Contact Name: (b) (6)					
Contact Title: (b) (6)				Contact e-mail address: (b) (6)	
<input checked="" type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		FDA establishment registration number: 2011171		<input type="checkbox"/> Manufacturer <input checked="" type="checkbox"/> Contract sterilizer <input type="checkbox"/> Contract manufacturer <input type="checkbox"/> Repackager/ relabeler	
Company/institution name: (b) (4)			Establishment registration number: 2011171		
Division name (if applicable): N/A			Phone number (include area code): (b) (4), (b) (6)		
Street address: (b) (4)			Fax number (include area code): (b) (4)		
City: (b) (4)		State/Province: (b) (4)		Country: USA	
ZIP/Postal Code: (b) (4)					
Contact Name: (b) (4), (b) (6)					
Contact Title: (b) (4), (b) (6)				Contact e-mail address:	
<input type="checkbox"/> Original <input type="checkbox"/> Add <input type="checkbox"/> Delete		FDA establishment registration number:		<input type="checkbox"/> Manufacturer <input type="checkbox"/> Contract sterilizer <input type="checkbox"/> Contract manufacturer <input type="checkbox"/> Repackager/ relabeler	
Company/institution name:			Establishment registration number:		
Division name (if applicable):			Phone number (include area code): ()		
Street address:			Fax number (include area code): ()		
City:		State/Province:		Country:	
ZIP/Postal Code:					
Contact Name:					
+Contact Title:			Contact e-mail address:		

5
4

Conceptus.

April 19, 2002

(b) (6)

Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

RE: Original Pre-Market Application (PMA)
Conceptus Essure™ System for Permanent Birth Control
PMA Shell Number: M010031- PMA
Expedited Review Request

Dear (b) (6) :

Conceptus, Inc. is submitting this Pre-Market Approval Application (PMA) for the Essure™ System, which is intended for use in women who are seeking permanent birth control (female sterilization). In accordance with Section 515(d)(5) of the Act, we are requesting Expedited Review of this PMA. The rationale to support the request follows this letter.

The Pre-Market Application has been submitted to the Agency in Modular format. The PMA Shell Plan was approved by the FDA on November 28, 2001 (M010031). A copy of the approved PMA Shell is attached to this letter.

Table 1 below, lists the Modules that have been submitted, their content, submission date and current status:

(b) (4)



Table 2 below, lists the contents of the PMA and references sections that were provided in earlier Modules:

Required PMA Sections	Where Submitted (Volume # in PMA)
CDRH Submission Cover Sheet	All Modules and PMA (Volume 1)
Checklist for Filing Decision for PMAs	PMA (Volume 1)
Submission Cover Letter	All Modules and PMA (Volume 1)
Table of Contents for PMA	All Modules and PMA (All Volumes)
Name and Address of Applicant	Module I
Description of Device, Functional Components/Ingredients, Device Properties, Principles of Operation	Module I
Performance Standards	N/A*
Animal Studies	Module I
Peri-hysterectomy Study	Module I
Non-Clinical Laboratory Studies	Module II
Hazard Analysis	Module II
Biocompatibility Studies	Module III
Pre-hysterectomy Study	Module III
Manufacturing Facility and Methods	Module IV
Sterilization Methods and Validation	Module IV
Shelf Life Studies and Proposed Shelf Life	Module IV
Phase II Study	Module V
O.U.S. Experience and Data	Module V
Summary of Safety and Effectiveness	PMA (Volume 1)
Pivotal Trial	PMA (Volume 2-11)
Single-Center Justification	N/A*
References (Pivotal Trial)	PMA (Volume 11)
Device Samples	PMA (Volume 12)
Proposed Labeling (Product/Professional/Patient)	PMA (Volume 12)
Professional Training Program	PMA (Volume 12)
Environmental Assessment	PMA (Volume 12)
Financial Disclosure and Certification	PMA (Volume 12)

* N/A: Not Applicable

Please note that the product name was changed from "STOP™" to "Essure™" after the completion of the Clinical Studies, but prior to this PMA application. As such, not all documentation referenced in this application reflects this change since it includes or references documents written prior to the name change. The device will be marketed under the new name, Essure™ System, when the PMA is approved.

CONFIDENTIAL

Conceptus, Inc.'s manufacturing facility is located at 1021 Howard Avenue, San Carlos, California, 94070. This facility is expected to be ready for an FDA Pre-Approval Inspection by June 15, 2002. Please note that this date has changed since the submission of our first two Modules (Module I and Module II), in which we stated May 1, 2002 as the date for the inspection.

In conformance with the National Environmental Act and 21 CFR §25.34(d), this PMA includes a claim of Categorical Exclusion.

The existence of this PMA application and the data and other information that it contains are confidential, and the protection afforded to such confidential information by 18 USC 1905, 21 USC 331(I), 5 USC 552, and other applicable laws is hereby claimed.

If there are questions regarding this submission, please contact me at (b) (6) via telephone, (b) (6) via fax, or at (b) (6) via e-mail, or contact (b) (6) via telephone, (b) (6) via fax, or at (b) (6) via e-mail.

Sincerely,

(b) (6)



Essure pbc (STOP Device) - Conceptus, Inc.

Module I Device Description & Early Animal/Clinical Studies

Proposed Submission Date: Nov. 15-21, 2001

CDRH Submission Cover Sheet
Conceptus Cover Letter
Table of Contents for Module I
Executive Summary of Module I

- General Information (Indication for Use)
- Device Description
 - ◆ General System Description
 - ◆ Functional Components
 - ◆ Key Design Parameters (Schematics and Photographs)
 - ◆ Properties Relevant to Treatment (Mechanism of Action)
 - ◆ Principles of Operation
 - ◆ Materials
 - ◆ Device Development Overview
- Animal Studies
 - ◆ Background
 - ◆ Proof of Concept Study (Rabbit)
 - ◆ Efficacy Study (Rabbit)
 - ◆ Mechanism of Action Study (Tissue reaction) (Rat)
- Peri-hysterectomy Clinical Study (STOP 10 protocol, G960052)
 - ◆ Background
 - ◆ Design of Clinical Trial
 - ◆ Clinical Protocol
 - ◆ Study Population and Period
 - ◆ Device Accountability
 - ◆ Number of Investigators/Number of Subjects per Investigator
 - ◆ Patient Tree
 - ◆ Discontinued patients
 - ◆ Demographics
 - ◆ Protocol Deviations
 - ◆ Inclusion/Exclusion Deviations
 - ◆ Clinical Trial Conduct
 - ◆ Safety/Adverse Events
 - ◆ Micro-Insert Placement Rate
 - ◆ Acute Occlusion/Anchoring
 - ◆ Conclusions Drawn from the Study
- Bibliography for Module I

Module II Hazard Analysis & Physical Testing (non-clinical)

Proposed Submission Date: Jan. 31-Feb. 7, 2002

CDRH Submission Cover Sheet
Conceptus Cover Letter
Table of Contents for Module II
Executive Summary of Module II

- Hazard Analysis (FMEA)
- Non-clinical laboratory studies for Physical & Chemical Performance
 - Bench Testing of STOP implant and delivery system
 - ◆ Anchoring
 - ◆ Flexibility
 - ◆ Navigation (Tracking)
 - ◆ Retraction
 - ◆ Deployment
 - ◆ Disengagement
 - ◆ Expansive Forces
 - Chemistry
 - ◆ Corrosion
 - MRI Compatibility
- Bibliography for Module II

10

Module III Material Safety and Mechanism of Action (Clinical)

Proposed Submission Date: Mar. 15-22, 2002

CDRH Submission Cover Sheet
Conceptus Cover Letter
Table of Contents for Module III
Executive Summary of Module III

- Biocompatibility/Toxicological Studies (non-clinical)
 - ◆ Cytotoxicity
 - ◆ Sensitization
 - ◆ Vaginal Irritation/Subchronic Toxicity
 - ◆ Acute Systemic Toxicity
 - ◆ Genotoxicity
 - ◆ Muscle Implantation (rabbit)
 - ◆ Chronic Toxicity
 - ◆ Mutagenicity
 - ◆ GLP compliance statement

- Pre-hysterectomy Clinical Study (IDE G960206)
 - ◆ Study purpose, protocol
 - ◆ Inclusion/exclusion criteria
 - ◆ Number of investigators/subjects per investigator
 - ◆ Study population and period/Demographics
 - ◆ Patient tree
 - ◆ Safety, adverse events
 - ◆ Occlusion/expulsion
 - ◆ Histology (based on 30 study subjects)
 - ◆ Device placement rate
 - ◆ Justification for use of foreign data
 - ◆ GCP Compliance Statement
 - ◆ Conclusions drawn from the study

- Bibliography for Module III

Module IV Manufacturing & Shelf-life & Validation

Proposed Submission Date: Apr. 15-22, 2002

CDRH Submission Cover Sheet
Conceptus Cover Letter
Table of Contents for Module IV
Executive Summary of Module IV

- Manufacturing Information
 - ◆ Critical/Non-Critical Device Status
 - ◆ Organization and Personnel (Employee Training)
 - ◆ Quality Assurance Program
 - ◆ Quality Audits
 - ◆ Buildings and Environments
 - ◆ Equipment
 - ◆ Acceptance and Control of Components
 - ◆ Production and Process Controls (Including specific Process Validation)
 - ◆ Document Control
 - ◆ Packaging and Labeling Control
 - ◆ Holding, Distribution, Installation
 - ◆ Device Evaluation (Finished device inspection and testing, and sampling plan based on a statistical rationale)
 - ◆ Records
 - ◆ Sterile Devices
 - Microbiological Studies (Bioburden Testing, Bacteriostasis and Fungistasis Analysis, Biological Indication (BI) Population Verification, EtO Residuals)
 - ◆ Devices Containing Software (Not applicable)
- Device Sterilization, Methods and Data
- Accelerated Aging & Real-time Aging, Proposed Shelf Life
 - ◆ Environmental and Shipping Validation
- Bibliography for Module IV

Module V Clinical Studies (Phase II and O.U.S.)

Proposed Submission Date: Apr. 15-22, 2002

CDRH Submission Cover Sheet
Conceptus Cover Letter
Table of Contents for Module V
Executive Summary of Module V

- Phase II Clinical Study (IDE G980152)
 - ◆ Study purpose, protocol
 - ◆ Inclusion/exclusion criteria
 - ◆ Number of investigators/subjects per investigator
 - ◆ Study population and period/Demographics
 - ◆ Patient tree
 - ◆ Device placement rate
 - ◆ Safety/comfort of device placement procedure
 - ◆ Recovery from device placement procedure^f
 - ◆ Safety/*in situ* comfort, adverse events
 - ◆ Occlusion/expulsion
 - ◆ Pregnancy
 - ◆ Justification for use of foreign data
 - ◆ GCP Compliance Statement
 - ◆ Conclusions drawn from the study

- Out of the U.S. Studies/Data
 - ◆ O.U.S. Marketing Experience
 - Identification of countries
 - Number of devices shipped
 - Adverse events/complaints
 - ◆ O.U.S. Post-Market Studies
 - Identification of countries
 - Study purpose and Protocol
 - Inclusion/exclusion criteria
 - Number of Investigators/subjects per Investigator
 - Study population and period/Demographics
 - Patient tree
 - Device placement rate
 - Safety/comfort of device placement procedure
 - Recovery from device placement procedure
 - Safety/comfort of device wearing
 - Occlusion
 - Pregnancy
 - GCP Compliance Statement
 - Conclusions drawn from the study

- Bibliography for Module V

PMA Application

Proposed Submission Date: Apr. 15-22, 2002

<u>Where Submitted</u>	<u>PMA Component</u>
Module I	● Name & address of Applicant
All Modules	● Table of Contents
PMA	● Summary of Safety & Effectiveness
Module I	● Description of Device, Functional Components/Ingredients, Device Properties, Principles of Operation
Module IV	● Manufacturing Methods
Module IV	● Sterilization Methods
Module IV	● Shelf Life Studies and Proposed Shelf Life
N/A	● Performance Standards: 514 standards or standards under the Radiation Control for Healthy & Safety Act (not applicable)
	◇ <u>Technical Sections</u>
Module II	● Non-Clinical Laboratory Studies
Module III	● Biocompatibility Studies
Module I	● Animal Studies
	◇ <u>Clinical Investigations</u>
Module I	● Peri-hysterectomy Studies
Module III	● Pre-hysterectomy Studies
Module V	● Phase II Studies
Module V	● Out of the U.S. Studies/Data
PMA	● Pivotal Trial
N/A	● Single-center Justification (not applicable)
All Modules	● Bibliography
PMA	● Device samples
PMA	● Proposed Labeling
PMA	● Professional labeling (including operation & instruction manual)
PMA	● Patient labeling
PMA	● Professional training program
PMA	● Environmental assessment
PMA	● Financial certification or disclosure (Part 54)
PMA	● Other information

EXPEDITED REVIEW REQUEST

Section 515(d)(5) of the act, as modified by Section 202 of the FDA Modernization Act of 1997, provides for “Special Review for Certain Devices”. This section of the Act is intended to provide a “more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions”. Accordingly, review priority is to be granted for devices: 1) representing breakthrough technologies, 2) for which no approved alternatives exist, 3) which offer significant advantages over existing approved alternatives, or 4) the availability of which is in the best interest of patients.

(b) (4)



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(b) (4)

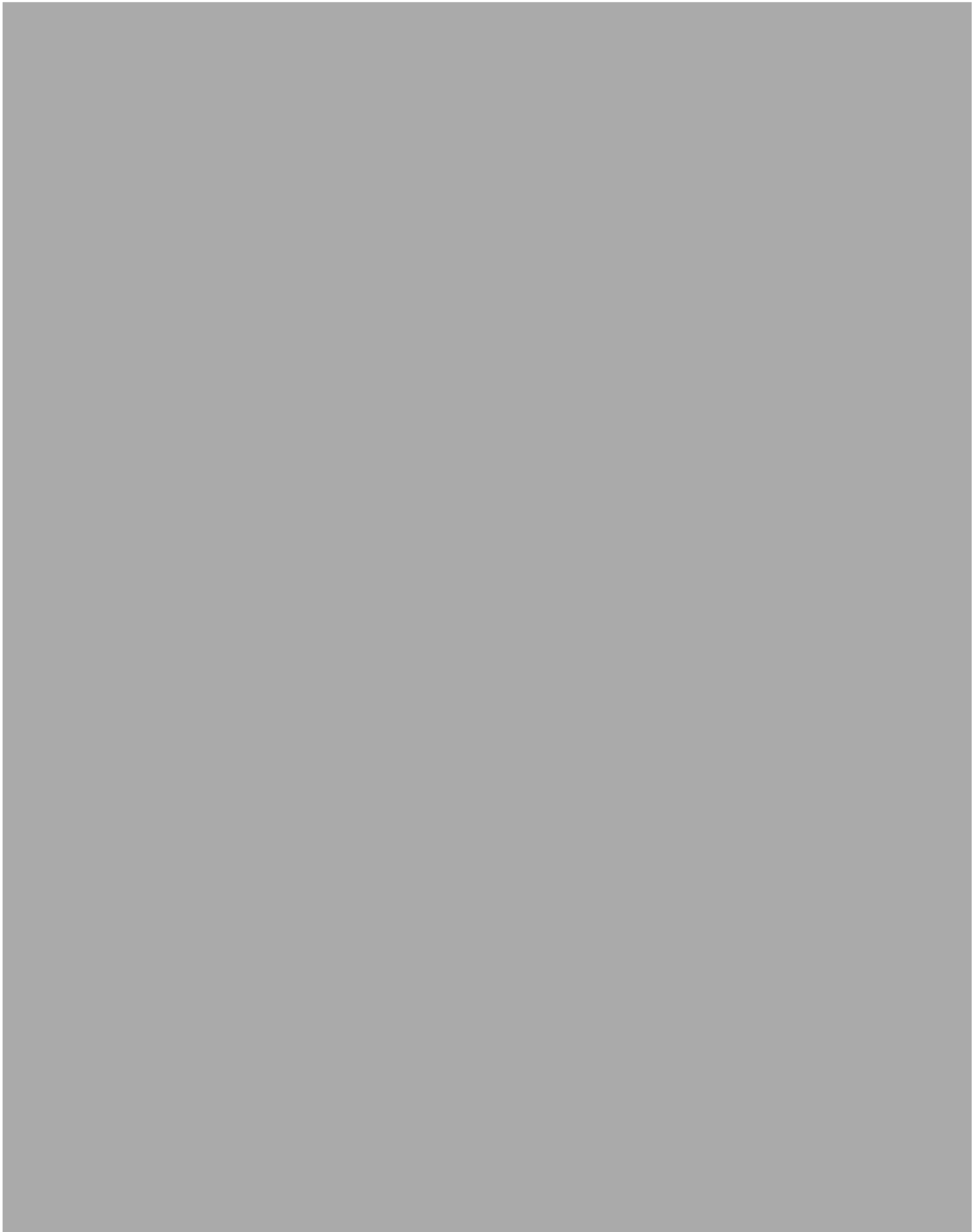


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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov

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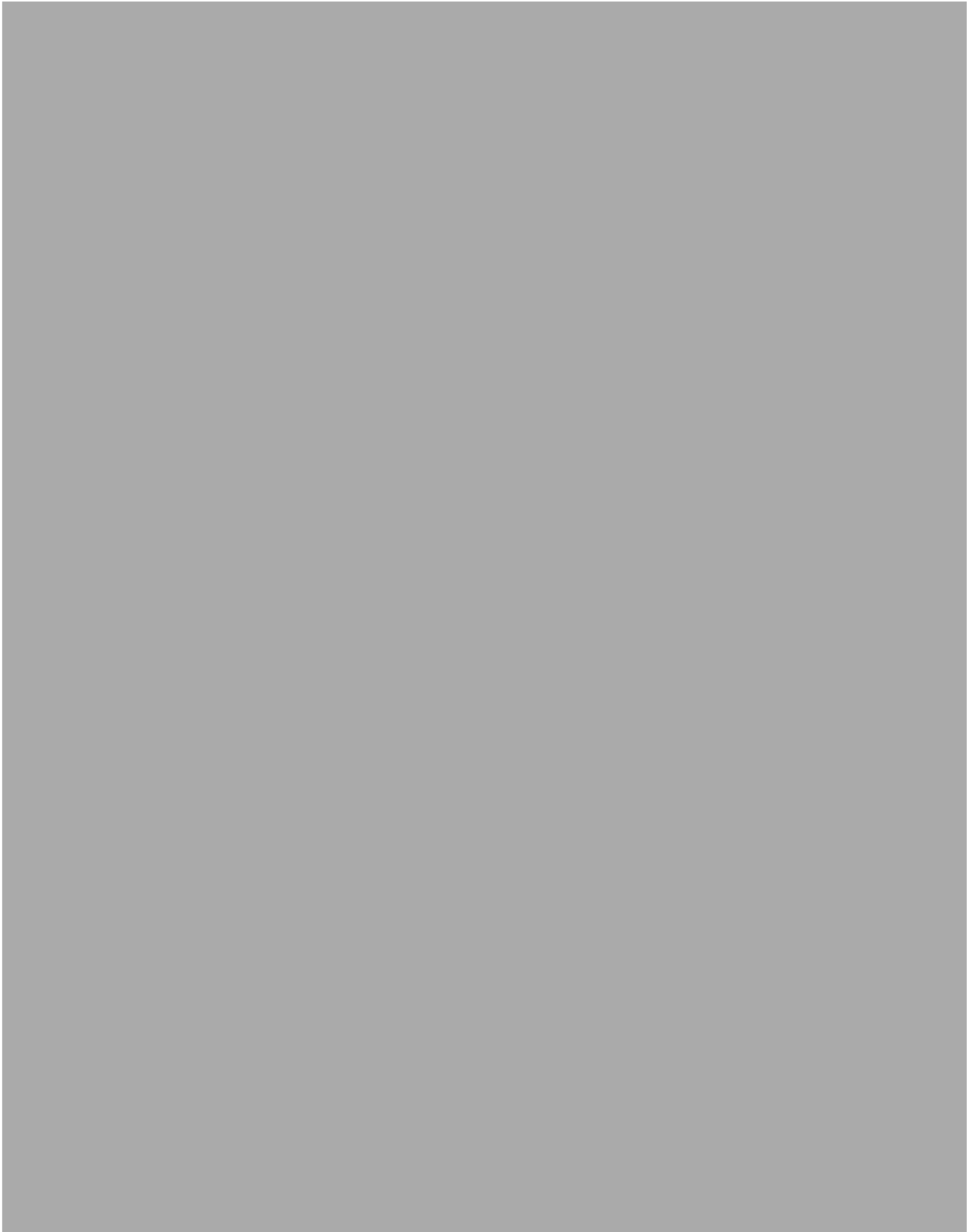


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Conceptus Essure™ System

Pre-Market Approval Application

(PMA)

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- VI. Financial Disclosure and Certification

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NOTE: This Checklist has been modified by Conceptus, Inc. to assist FDA with the review of the Essure System PMA (M010031). A column has been added to the following tables to show the location of each 'Filing Review Element' within the PMA Shell.

CHECKLIST FOR FILING DECISION FOR PMAs
Revised Date: 4-28-00

Identification:

PMA Number: _____ **Date Received:**

Sponsor:

Device:

Division/Branch:

Decision:

Recommendation: File __ **Not File**

Administrative Reviewer Signature: _____ **Date:**

Supervisory Signature: _____ **Date:**

Administrative:

Tier: I II III

Expedited Review: Yes No

Procode:

THE PMA CHECKLIST FOR FILING DECISION**PART A- DEFICIENCIES TO BE INCLUDED AS REASONS FOR NOT-FILING THE PMA**

Filing Review Elements	Yes	Where Submitted	Not Applicable
I. Organizational and Administrative Elements (21 CFR 814.20, Blue Book Memo #P-90-2)	↓	↓	↓
A. Are key administrative items present? CFR 814.20(a), 814.20(b)(1) and 814.20(b)(2))	✓	Module I All Modules	
B. Is PMA organization sufficient to permit substantive review?	✓		
C. Is device appropriate for review in class III?	✓		
D. The regulations do not allow the FDA to file a PMA if a 510(k) for the same device is pending. Has the applicant withdrawn any pending 510(k)? If no stop review! (21 CFR 814.42(e)(3))			✓
E. If this device has been the subject of an NSE decision, does the PMA address the NSE issues (e.g., new material, energy source, etc.)?			✓
F. Are you aware of the applicant being the subject of an integrity investigation? If yes, consult the ODE integrity officer. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2, 21 CFR 814.42(e)(4) and Federal Register 90N-0332, September 10, 1991)			✓

G. Is there is a prior history of sponsor with this device? For example, has a previously submitted PMA for this device been withdrawn? If yes, does the current PMA address any historical issues related to fraud, safety, or effectiveness?			✓
II. Do the data submitted in support of this PMA constitute valid scientific evidence? (21 CFR 860.7)	✓	PMA Volume 2 (Section I)	
III. Summary of Safety and Effectiveness Data (Blue Book Memo #P86-1)	↓	↓	↓
A. Are indications for use provided?	✓	PMA Volume 1 (SSE)	
B. Is an abbreviated device description provided?	✓	PMA Volume 1 (SSE)	
C. Is a summary of the studies provided? (21 CFR 814.20(b)(3))	✓	PMA Volume 1 (SSE)	
1. Is a summary of the non-clinical laboratory studies and results provided?	✓	PMA Volume 1 (SSE)	
2. Is a summary of the clinical investigations and results provided?	✓	PMA Volume 1 (SSE)	
D. Are conclusions drawn from the studies provided? (21 CFR 814.20(b)(3)(vi))	✓	PMA Volume 2 (Section I)	

1. Is a discussion demonstrating that PMA information provides reasonable assurance of the safety and effectiveness of the device for its intended use provided?	✓	PMA Volume 2 (Section I)	
2. Is a risk/benefit analysis provided?	✓	PMA Volume 2 (Section I)	
IV. Labeling (21 CFR 814.20(b)(10) and Blue Book Memo #P91-4)	↓	↓	↓
A. Has appropriate draft labeling been submitted (e.g., Physician, Patient, Technical, etc.)?	✓	PMA Volume 12 (Section III)	
V. Device Characteristics and Manufacturing Sections (Note: may be waived for filing purposes and submitted later during the substantive review period; OCS reviews prior to QSR inspection for QSR issues; ODE reviews for safety and Effectiveness issues) (21 CFR 814.20(b)(4)(v) and Guidance for the Preparation of PMA Manufacturing Information)	↓	↓	↓
A. Is a description of device, pictorial representations, and materials specifications present? (21 CFR 814.20(b)(4)(i))	✓	Module I	
B. Is a description of the principles of operation of the device (including components) and properties relevant to clinical function present? (21 CFR 814.20(b)(4)(iii))	✓	Module I	
VI. Nonclinical Laboratory Studies (21 CFR 814.20(b)(6)(i))	↓	↓	↓
A. Microbiological	✓	Module IV	
B. Toxicological	✓	Module III	
C. Immunological			✓

D. Biocompatibility	✓	Module III	
E. Stress	✓	Module II	
F. Wear	✓	Module II	
G. Shelf life	✓	Module IV	
H. Analytical (for IVDs)			✓
I. Have other pertinent device/material-specific laboratory animal tests have been provided?	✓	Module I	
J. Has the applicant provided documentation to establish conformance with applicable standard and/or FDA guidance/guidelines? (21 CFR 814.20(b)(5))			✓
VII. Clinical Investigations (21 CFR 4.20(b)(6)(ii))	↓	↓	↓
A. Is there an adequate description of clinical utility? (Blue Book Memo #91.1)	✓	PMA Volume 2 (Section I)	
B. If the PMA is supported by a sole investigator, has a justification been provided? (21 CFR 814.20(b)(7))			✓
C. Are clinical protocols described and included?	✓	PMA Volume 2 (Section I)	
1. Are numbers of investigators and subjects per investigator specified?	✓	PMA Volume 2 (Section I)	
2. Is a description of subject inclusion and exclusion criteria provided?	✓	PMA Volume 2 (Section I)	
3. Has a description of the study period been provided?	✓	PMA Volume 2 (Section I)	

4. Have clinically significant endpoints been selected?	✓	PMA Volume 2 (Section I)	
D. Was safety and effectiveness data provided? (21 CFR 814.20(b)(6)(ii))	✓	PMA Volume 2 (Section I)	
1. Was the clinical study completed as specified in the protocol (e.g., number of patients completing the study, follow-up period, follow-up evaluations, single device design, etc.)?	✓	PMA Volume 2 (Section I)	
2. Is a description of study population demographics provided?	✓	PMA Volume 2 (Section I)	
3. Is a description of adverse events, e.g. adverse reactions, complaints, discontinuations, failures, replacements, etc. given?	✓	PMA Volume 2 (Section I)	
4. Are statistical analyses of the clinical investigations provided?	✓	PMA Volume 2 (Section I)	
5. Have all appropriate FDA requirements applicable to the device and/or clinical study been met?	✓	PMA Volume 2 (Section I)	
6. Are foreign clinical data included? If yes, are data justified and acceptable? (21 CFR 814.15(b) and 814.15(d))	✓	PMA Volume 2 (Section I)	
7. Has all information reasonably known to the sponsor and relevant to the safety and effectiveness evaluation been provided? (21 CFR 814.20(b)(8)(ii))	✓	PMA Volume 2 (Section I)	

E. Has documentation and conformance with applicable standard and/or FDA guidance/guidelines been provided? (21 CFR 814.20(b)(5))			✓
F. Does the OST Statistician recommend filing?		FDA	
G. Have report forms for patients who died or were discontinued been provided, i.e., to resolve potential bias? (Goal: 100% accountability)		No Deaths	✓
H. Has the applicant complied with the requirements of 21 CFR Part 54 regarding financial disclosure of clinical investigators?	✓	PMA Volume 12 (Section VI)	
VIII. Is there any other reason not addressed above which should be identified as a reason for not filing the PMA? If so, briefly explain:		FDA	
PART B – DEFICIENCIES TO BE INCLUDED IN THE “MINOR” SECTION OF THE NOT- FILING OR FILING A PMA			
Additional Filing Review Elements	Yes	Where Submitted	Not Applicable
IX. Additional Administrative and Organizational Elements			
A. If there are color additive considerations has an <u>attempt</u> been made to document them? (21 CFR 814.20(f))			✓
B. Is a bibliography provided? (21 CFR 814.20(b)(8)(i))	✓	PMA Volume 11	
C. Do we need a device sample? If yes, has it been provided? (21 CFR 814.20(b)(9))	✓	PMA Volume 12 (Section II)	

X. Additional Regulatory Requirements			
A. Have alternative practices been included and described? (21 CFR 814.20(b)(3)(iii))	✓	PMA Volume 1 (SSE)	
B. Is the description of prior marketing history provided? (814.20(b)(3)(iv))	✓	PMA Volume 1 (SSE)	
C. Was the clinical study conducted in compliance with Part 56 (IRB), Part 50 (Informed Consent), or Parts 812 or 813 (IDE)? (21 CFR 814.20(b)(6)(ii)(A)and(B))	✓	PMA Volume 2 (Section I)	
D. Has the data presented in the PMA taken into account the staff concerns addressed in the IDE?	✓	PMA Volume 2 (Section I)	
E. Is reference to applicable IDEs given? IDE# _____	✓	PMA Volume 2 (Section I)	
PART C- ADDITIONAL CONSIDERATIONS			
XI. Additional Considerations			
A. Can the QSR inspection be initiated within an appropriate timeframe? If the manufacturing section has been waived or the manufacturing site(s) are not currently ready for inspection, check the NO box.	✓	After June 15, 2002	
B. Are there any special administrative issues? If so, explain:		FDA	
C. Are there any precedent setting substantive issues? If so, explain.		FDA	

P020014/V2/C1

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Section I. Clinical Data Report: Pivotal Trial

A. Executive Summary

Introduction

Provided in this introductory section is a description of the unintended pregnancy and abortion rates in the United States as well as the complications associated with pregnancy, the documented need for contraceptive alternatives, a discussion of the risks associated with current methods of permanent birth control (female sterilization), and the unique characteristics of the Essure System for Permanent Birth Control.

Unintended Pregnancy/Abortion Rates

Unintended pregnancy is a significant public health issue that affects not only the woman involved, but also society as a whole. The significance of this public health need is evidenced by the signing into law of Title X of the Public Health Service Act, which provides for a comprehensive federal program devoted entirely to providing family planning services on a national basis.

Using data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, it has been estimated that almost half (48%) of all pregnancies in the United States in 1994 were unintended, and 54% of these ended in abortion¹. In 1994 alone, there were an estimated 3,000,000 unintended pregnancies, with an estimated half (48%) of women aged 15-44 having had at least one unplanned pregnancy sometime in their lives¹. Although teenagers have the highest rate of unintended pregnancy,

¹ Henshaw SK. Unintended Pregnancy in the United States. Family Planning Perspectives, 1998, 30(1): 24-29 & 46.

the second highest rate is found in women aged 40-44². Furthermore, the rate of unintended pregnancies in the U.S. has declined little over the past several decades, and remains higher than other developed nations².

In 1997, over one million abortions were performed, and an estimated 43% of women will have at least one abortion by the time they are 45 years old¹.

Abortion is not just an issue that faces teenagers. In fact, based on a 1994-1995 national survey of almost 10,000 abortion patients, over 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women who were age 30 or over³.

Maternal Risks of Pregnancy

According to the CDC⁴, approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Two to three women die each day from a pregnancy-related complication, and the maternal mortality rate has not declined since 1982⁴. The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy. It should be noted that the risk of pregnancy-related death rises after the age of 35⁵. In addition to mortality resulting from pregnancy, the CDC states that more than one in three pregnant women in the U.S. develop a pregnancy-related complication⁴. The most common complications include: miscarriage, ectopic pregnancy, hemorrhage, infection, diabetes, high blood pressure, excessive vomiting, premature labor, need for Caesarean delivery, and depression. Furthermore, based on 1986-1987 data from the National Hospital Discharge Survey (NHDS), an estimated 22.2 per 100 hospitalizations involving a birth were non-delivery

² Global Health Options.

³ Henshaw SK. Abortion Patient in 1994-1995: Characteristics and Contraceptive Use. *Family Planning Perspectives*, 28: 140-147 & 158, 1996.

⁴ CDC's Reproductive Health Information Source. *Safe Motherhood: Promotion Health for Women Before, During, and After Pregnancy 2002*.

⁵ CDC Press Release: Fact Sheet, Pregnancy-Related Mortality.

related hospitalizations of pregnant women⁶. Hospitalization for a pregnancy-related complication required an average of >2 million hospital days of care per year and cost >1 billion dollars annually⁶. The authors of this study provided a nationwide estimation of serious pregnancy-related morbidity following childbirth: 62,400 readmissions occurred during the postpartum period, yielding an average annual rate of 8.1 readmissions per 1,000 deliveries.

As stated by the CDC, childbirth remains the most common reason for hospitalization in the U.S., and complicated pregnancies result in more costly hospitalizations. Thus, since women who have unintended pregnancies are less likely to have appropriate prenatal care, more likely to have entry into prenatal care at a later stage of the pregnancy, and are at an increased risk of domestic violence⁷, they are presumably at higher risk of complications and account for more costs related to pregnancies.

Risks to Infant/Child

The National Commission to Prevent Infant Mortality has stated that: “Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception.”⁸ Similarly, a review by the U.S. Institute of Medicine of the research on this topic concluded that “the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development⁹. The CDC also states that an infant from an unintended pregnancy has an increased risk of low birth rate, neonatal mortality, risk of SIDS, and developmental problems⁷.

Clearly, there is a significant public health issue represented by these facts and figures.

⁶ Franks AL. Hospitalization for pregnancy complications, United States, 1986 and 1987. *Am J Obstet Gynecol* 1992; 166:1339-44.

⁷ Koonin LM. *Promoting Healthy Pregnancies: Counseling and Contraception*. September 20, 2000.

⁸ Alan Guttmacher Institute. *Title X and the U.S. Family Planning Effort*.

⁹ Alan Guttmacher Institute. *Family Planning Improves Child Survival and Health*. 1998.

Need for Contraceptive Alternatives

Based on data from the 1995 National Survey on Family Growth, it has been suggested in the literature that the high rates of unintended pregnancy reflect dissatisfaction with current methods¹⁰. In addition, based on a 64-country survey, it has been shown that the prevalence of contraceptive use rises with increased access to a variety of contraceptive methods¹¹.

The 1995 National Survey on Family Growth provided data on the current profile of contraceptive use in the United States based on a survey of almost 7,000 women. The survey revealed that the percentage of women discontinuing contraceptive use for method-related reasons within 12 months of method initiation was 44%¹⁰. In addition, during the lifetime of a typical woman who uses reversible methods of contraception, she will discontinue use for a method-related reason 9.5 times. If women using sterilization are included as well, the typical woman will discontinue use of a contraceptive for a method-related reasons only 7.2 times during her lifetime. The survey also found that the typical woman will experience 1.8 unintended pregnancies. If women using sterilization are included as well, the typical woman will experience 1.3 unintended pregnancies. The survey also noted that 6% of sexually active women were not using a contraceptive, which translates to approximately 3.5 million women at risk of unintended pregnancy. Indeed, of the 6 million pregnancies that occurred that year, nearly half were unintended, and more than half of these unintended pregnancies occurred among women who were using contraceptives.

The need for contraceptive alternatives has been acknowledged in recent years not only in the published literature, but also at meetings of the FDA's OB/GYN

¹⁰ Trussel J. Contraceptive Failure, Method-Related Discontinuation and Resumption of Use: Results from the 1995 National Survey of Family Growth. *Family Planning Perspectives*, 1999, 31(2): 64-72 & 93.

¹¹ Ross J. Contraceptive Method Choice in Developing Countries. *International Family Planning Perspectives*, 2001, 28(1): 32-40.

Advisory Committee. Additionally, the need for less invasive transcervical methods of sterilization has been a primary research focus for the USAID Office of Population, Family Health International (FHI), the CONRAD Program, and the WHO Human Reproduction Program.

In introductory remarks to the panel convened in October of 1996 for the review of the PMA for the Lea's Shield, Mr. Pollard (Chief, Obstetrics and Gynecology Devices Branch, FDA) stated: "I would like to add at this point that FDA is responsive to the concerns of women's advocacy groups across the U.S. Many of these groups are very concerned about the limited number of contraceptive options available to women and believe that FDA should be re-examining its review standards for evaluation of these products. This need for more contraceptive options was most recently emphasized in the report that just issued from the Institute of Medicine entitled 'Contraceptive Research and Development: Looking to the Future', highlighting the high rate of unintended pregnancies in the U.S. and worldwide."

In addition, the FDA convened a meeting of the panel in October of 1999 to discuss the requirements for vaginal barrier contraceptive devices to "recalibrate our premarket entry process and optimize the balance of premarket and postmarket requirements" for these devices, as stated by Mr. Pollard. This was largely driven by the results of the 1995 National Survey on Family Growth. Mr. Pollard presented to the panel some of the results discussed above from the survey regarding high rates of unintended pregnancy, abortion, and discontinuation of contraception due to method-related reasons, and went on to state: "To us, at FDA, that describes a huge unmet need." While the focus of the panel meeting was for vaginal barrier contraceptive devices rather than tubal occlusion devices, the underlying motivation for convening the meeting still pertains to consideration of the Essure System: the large unmet need in the area of contraceptive alternatives for women.

The author of the published findings of the 1995 Survey concluded that the high pregnancy rates in the survey “do not reflect the inherent efficacy of methods when used correctly and consistently, but instead reflect imperfect use because most reversible methods are difficult to use correctly.” The author went on to state: “such high rates of discontinuation almost surely reflect dissatisfaction with current methods.”

Prevalence of Tubal Sterilization

Currently, women must choose between temporary reversible methods, with all the limitations discussed above, and permanent birth control (sterilization), with its attendant invasiveness, morbidity, and mortality. Discussed below is the prevalence of tubal sterilization as a contraceptive choice, as well as the risks associated with this method.

Tubal sterilization is the most prevalent method of birth control in the United States. From 1994-1996, more than 2,000,000 tubal sterilizations were performed, for an annual incidence of 11.5 per 1,000 women, or 684,000 per year¹². As noted by (b) (6) at a recent meeting on transcervical sterilization sponsored by ARHP, this may well be an underestimate due to the difficulty in capturing the data in recent years.

All currently approved methods of tubal sterilization require access to the peritoneal cavity, and therefore carry the inherent risk associated with invasive surgery. Half of the tubal sterilizations are performed immediately post-partum and are done via mini-laparotomy or laparotomy¹³. The other half represent “interval” sterilizations, 89% of which are done laparoscopically¹³. Therefore, a slight majority of tubal sterilizations are performed by mini-

¹² MacKay AP. Tubal Sterilization in the United States, 1994-1996. *Family Planning Perspectives*, 2001, 33(4):161-166.

¹³ ACOG Technical Bulletin #222 – April 1996. Sterilization.

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laparotomy/laparotomy. Currently, laparoscopy is predominantly performed with general anesthesia and involves one or more punctures of the abdominal wall for insertion of a laparoscope; the tubal ligation procedure is then performed through the puncture sites in the abdomen. Both laparotomy and mini-laparotomy are more extensive procedures and require relatively longer recovery periods than laparoscopic methods. About 93 percent of the procedures in the U.S. are performed in a hospital or surgi-center under general anesthesia, with laparoscopic procedures requiring an average of 4-5 hours of hospital recovery time¹⁴, an average of 4-6 days before returning to regular activities, not including the day of surgery^{15,16}, and an average of 3 days before returning to work¹⁶. For procedures performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

Risks with Tubal Sterilization – Mini-Laparotomy/Laparotomy

The Centers for Disease Control and Prevention (CDC) CREST study¹⁸ reported on a subgroup of almost 300 women who underwent interval tubal sterilization by laparotomy. In this subgroup, a major complication rate of 5.7% was reported¹⁷, which was comprised of febrile morbidity and re-hospitalizations. Re-hospitalization occurred for the following reasons: pelvic abscess, pulmonary abscess, pulmonary embolus, bowel obstructions, staph wound infection at site of laparotomy incision, etc. The mean length of postoperative hospital stay was increased by 1.9 nights for women who had at least one complication as compared to those without complication¹⁷. This does not include the additional

¹⁴ Bordahl PE. Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study. *Obstet Gynecol* 1993; 81: 137-41.

¹⁵ Fraser RA. The prevalence and impact of pain after day-care tubal ligation surgery. *Pain* 39 (1989) 189-201.

¹⁶ Garcia FA. Economic and Clinical Outcome of Microlaparoscopic and Standard Laparoscopic Sterilization, A Comparison. *J Reprod Med* 2000; 45:372-376.

¹⁷ Layde PM. Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy. *Obstet Gynecol* 62:180, 1983.

¹⁸ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-70.

hospitalization experienced by women who were readmitted following their initial discharge. The mean total convalescence period from the time of the surgery until the resumption of normal activities was increased by 8.3 days (from 9.6 days) among women experiencing a complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparotomy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (1.8%), primary incision complications (12.6%), infections (1.1%), and “other” (3.3%). The total complication rate in this study, for the complications reported, was 18.8%. In a similar study comparing the Filshie Clip with the Tubal Ring under laparotomy²⁰, the following complications were noted: surgical injuries (7.3%), primary incision complications (13.9%), infections (0.9%), and “other” (1.4%). The total complication rate in this study, for the complications reported, was 23.5%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional approach.

Risks with Tubal Sterilization – Laparoscopy

Based on data from the CREST study involving over 9,000 women who underwent tubal sterilization by laparoscopy, major complications occurred at a rate of 1.6%, with unintended laparotomy as the most frequent complication²¹. Laparotomies were performed for the following reasons: unexpected bleeding, hematoma formation, viscous perforation (stomach and bowel), and fallopian tube resection. Rehospitalization occurred for the following reasons: pelvic infections, heavy vaginal bleeding, abdominal/pelvic pain, urinary tract infection,

¹⁹ Dominik R. Two Randomized Controlled Trials Comparing the Hulka and Filshie Clips for Tubal Sterilization. *Contraception* 62 (2000) 169-175.

²⁰ Sokal D. Two Randomized Controlled Trials Comparing the Tubal Ring and Filshie Clip for Tubal Sterilization. *Fertility and Sterility*. Vol 74, No 3, September 2000.

²¹ Jamieson DJ. Complications of Interval Laparoscopic Tubal Sterilization: Findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol* 2000; 96:997-1002.

peritonitis caused by bowel burn, bowel obstruction, etc. In an early report based on the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, the median postoperative hospital stay increased from 0 nights for women with no complications to 2 nights for women who had at least 1 complication²². The occurrence of a complication also increased the median total convalescence from 4 days to 14 days. More than one third (36%) of women who developed a complication had a total convalescence longer than 21 days, compared to only 2% of women with no complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparoscopy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (0.8%), primary incision complications (7.9%), infections (0.08%), and “other” (2.5%). The total complication rate in this study, for the complications reported, was 11.2%. In a similar study comparing the Filshie Clip with the Tubal Ring via laparoscopy²⁰, the following complications were noted: surgical injuries (2.2%), primary incision complications (4.4%), infections (0.4%), and “other” (1.0%). The total complication rate in this study, for the complications reported, was 8%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional method.

Finally, a large prospective study involving over 24,000 women who underwent tubal ligation using one of 5 methods²³ was conducted. In this study, the rate of surgical difficulties, which included anesthesia and equipment problems, etc., ranged from 2.4% to 12.5% (5.1% overall). The rate of surgical complications, which included uterine perforation, bowel injury, artery/vein injury, bladder injury, ovarian injury, etc., ranged from 0.7% to 2.7% (1.7% overall). The rate of

²² Destefano F. Complications of Interval Laparoscopic Tubal Sterilization. *Obstet Gynecol* 61:153, 1983.

²³ Bhiwandiwalla PP. A Comparison of Different Laparoscopic Sterilization Occlusion Techniques in 24,439 Procedures. *Am J Obstet Gynecol* 144:319, 1982.

technical failures, which required a change to a different technique or abandoning the procedure, ranged from 0.6% to 1.0% (0.8% overall).

Risks of Tubal Sterilization – Local vs. General Anesthesia

Based on early reports of the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, a fivefold difference in complication rates was found between procedures performed under general anesthesia and those performed under local anesthesia²². In subsequent reports from the CREST study involving over 9,000 women, use of general anesthesia was found to be a predictor of complications in women undergoing interval laparoscopic tubal sterilization²¹. In addition, 40% of the deaths attributable to tubal sterilization followed complications associated with general anesthesia, and there were no deaths due to complications from local anesthesia²⁴.

In a randomized, controlled trial comparing tubal ligation performed under local anesthesia to general anesthesia in 125 women, total procedure/post-surgery time was significantly shorter in the local anesthesia group¹⁴. In addition, the general anesthesia group had significantly more abdominal pain during the hospital stay, and use of analgesics immediately after surgery was more extensive. Also, the “awakeness” score was higher in the local anesthesia group the same evening as the procedure. Similar to these findings, in another randomized study comparing laparoscopic tubal ligation performed under local vs. general anesthesia²⁵, women in the local anesthesia group had a slightly shorter anesthesia time and recovery room stay. In addition, women in the general anesthesia group were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate of 110 or higher.

²⁴ Peterson HB. Deaths Attributable to Tubal Sterilization in the United States, 1977 to 1981. *Am J Obstet Gynecol* 146:131, 1983.

²⁵ Peterson HB. Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study. *Obstet Gynecol* 70:903, 1987.

Although use of local anesthesia for tubal sterilization is associated with a lower rate of complications, laparoscopic tubal sterilization still requires access to the peritoneal cavity with its associated risks.

Tubal Sterilization Risks – Pain/Return to Normal Activities

Finally, in a study of over 50 women using validated measures to assess the incidence, intensity and duration of pain following tubal ligation performed laparoscopically, it was found that 85% of women reported that pain and/or fatigue impacted their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of the procedure. The most powerful predictor of return to normal activity was the total amount of pain experienced. A separate study of 50 women undergoing laparoscopic tubal sterilization similarly found that the average number of days to resume normal activities was 4-6¹⁶. Also, as stated above, when tubal sterilization is performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

A New Contraceptive Alternative – The Essure System

Given the high unintended pregnancy, abortion and discontinuation rates associated with temporary methods of birth control, and the significant complications that can occur with the invasive surgery currently required for permanent birth control, we believe that women would benefit from a new contraceptive alternative that offers a less invasive method to achieve permanent birth control. As evidence of patient interest in such an alternative, is the statement made by a patient advocacy group to the FDA's OB/GYN Advisory Committee (panel). In February of 1996, Ms. Cindy Pearson, Program Director of the National Women's Health Network addressed the panel, which was convened to review the PMA for the Filshie Clip, stating: “. . .So we just wanted

to communicate a general sense that women are interested in alternative methods of sterilization. In particular, women are interested in methods that offer a safety or convenience advantage over the methods that are currently available to them. . .”.

The Essure System offers transcervical placement of the Essure Micro-insert, which can be accomplished without incisions or general anesthesia, with no loss of method effectiveness as compared to incisional tubal sterilization. Since the data that follow in this report demonstrate that this can be done safely and effectively to provide permanent birth control, we believe that this alternative will be embraced by women and their physicians, and will offer a significant public health benefit as a result.

Summary

In summary, due to the following points, we believe that there is strong evidence of the need for a new contraceptive alternative for women, especially a permanent method that can be performed without incisions or general anesthesia:

- An estimated half (48%) of pregnancies that occur in the United States each year are unintended, translating to an estimated 3,000,000 unplanned pregnancies in the United States each year.
 - The age group that has the second highest rate of unintended pregnancy is women aged 40-44.
- An estimated half of all unintended pregnancies result in abortion, translating to an estimated 1,000,000 abortions each year in the United States.
 - 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women over 30 years old.

- The morbidity associated with pregnancy is not infrequent or insignificant to the women or to society.
- There has been a documented risk to infants and children due to unintended pregnancies.
- Deaths and major complications occur with currently available methods of tubal sterilization due to general anesthesia and invasion of the peritoneal cavity that is associated with current methods.

We believe that many of the unintended pregnancies and abortions each year could be avoided if women had a permanent birth control option with an alternative risk/benefit profile than current methods.

Executive Summary of Clinical Data

Detailed data on the Pivotal Trial conducted to establish a reasonable assurance of safety and effectiveness for the Essure System are provided in the following sections. This section provides an Executive Summary of the data.

Placement Rates

Of the 507 women in the Device Evaluation population, bilateral placement was achieved in 464 (92%), and single Micro-insert placement was achieved in 2 women with a unicornuate uterus (100%). Of the 41 (8%) women with bilateral tubes who did not achieve bilateral placement, 15 (37%) were found to have proximal tubal occlusion (PTO) on follow-up HSG. Eliminating these women from the analysis of placement rates results in an overall bilateral placement rate of 464/494 (94%).

Satisfactory Micro-Insert Location/Occlusion Rates

A total of 456/464 women with bilateral placement completed the 3-month post-device placement visit and underwent an HSG. Of those 456 women, 437 (96%) were noted on HSG to have Micro-inserts in satisfactory location. Of those 437 women, 421 (96%) were also noted to have bilateral tubal occlusion. Nine of the women with Micro-inserts in unsatisfactory location (expulsion due to improperly placed Micro-insert) returned for a second placement procedure to replace the expelled Micro-insert. All achieved bilateral placement and were found on follow-up HSG to have bilateral occlusion and Micro-inserts in satisfactory location. All of the 16 women who had tubal patency at the initial HSG chose to undergo a second HSG 3 months later, and all were found to have bilateral occlusion on the second HSG. Therefore, of the 456 women with bilateral placement completing the 3-month visit, 446 (98%) were ultimately found to have Micro-inserts in satisfactory location and bilateral occlusion.

Reliance Rates

As stated above, 446/456 women (98%) with bilateral placement were able to rely on Essure for contraception. In addition, 2 women with bilateral placement did not have an HSG but chose to begin relying on Essure. Also, four women with unilateral placement and either confirmed contralateral PTO (2) or a unicornuate uterus (2) were able to rely on Essure for contraception. Among the 507 women in whom an Essure System was used, 452 (89%) were ultimately able to rely on Essure for contraception.

Adverse Event Rate

Adverse events on the day of the placement procedure occurred in 17 (3%) women. All events were resolved prior to the woman being discharged, except for one woman who required overnight observation following an adverse reaction

to pain medication. Day of procedure events included the following, all of which occurred in <1% of cases: vomiting, vaso-vagal response, hypervolemia, band detachment, perforation, excessive vaginal bleeding, and “other” (skin itching, bloating, loss of appetite, and reaction to saline used for uterine cavity distension).

Adverse events reported at the 3-month post-device placement visit that *initially* prevented the woman from relying on Essure occurred in 20 (4%) women. These were primarily Micro-insert expulsions following original Micro-insert placement that was out-of-specification. Nine of the 14 women who experienced an expulsion chose to undergo a second placement procedure, and all were successful. Therefore, including the perforation that was diagnosed on the day of placement, adverse events that *ultimately* prevented reliance occurred in only 12 (2%) women. The most frequently reported adverse events reported in the first year that did not prevent the woman from relying on Essure, but were rated by the Investigator as at least “possibly” related to Essure were back pain (8.6%), abdominal pain/cramps (4.2%) and uncharacterized pain/discomfort (3.2%). All other events occurred in less than 3% of women.

Patient Satisfaction/Comfort

Women in the study consistently rated their overall satisfaction and comfort in wearing the Micro-inserts as very high. At all study visits, 99% of women rated their comfort with wearing Essure as “good” to “excellent”. At all study visits, at least 98% of women rated their overall satisfaction as somewhat to very satisfied (this included women who were not able to rely on Essure).

2)

Pregnancy Prevention

There have been no pregnancies in any of the 452 women who are currently relying on Essure for contraception. There are 361 women with bilateral placement in the Pivotal Trial who have been followed for at least one-year after relying on Essure for contraception. The remaining women have completed from 5-11 months of follow-up. Combined with data from the Phase II study, this equates with over 620 women-years of first year effectiveness evaluation (and 167 woman-years of second year evaluation). The current estimate of the one-year effectiveness rate based on these data is 99.8%.

Summary

In summary, we believe that the data contained in this Pivotal Trial Report, together with the data provided elsewhere in the PMA, provide a reasonable assurance of the safety and effectiveness of the Essure System.

B. Background

Four separate studies of the Essure System were conducted as part of the clinical development of the product. Each is depicted in the graphic below.

(b) (4)



The reports of the first 3 studies were included in PMA Module I, Module III and Module V, respectively. Unlike prior clinical trials, the Pivotal Trial included evaluation of the gamma design only.

The IDE for the Pivotal Trial of the Essure System (G000055) was submitted to the FDA on February 28, 2000, following a pre-IDE meeting on November 19, 1999. Conditional IDE approval was received on March 24, 2000, and final IDE approval was received on September 7, 2000.

It should be noted that this report reflects the study protocol and statistical plan that were approved under the IDE. Approximately 10 months after final IDE approval, on June 29, 2001, a Determination/Agreement meeting was held with the Agency to make binding the agreements reached during the IDE approval process. Binding agreement was reached for the majority of the earlier agreements under the IDE. The two exceptions were: 1) filing the PMA if only a 95% effectiveness rate was established, and 2) use of the CREST study as a historical control. Agreement to use the CREST study as a “qualitative benchmark” as opposed to a statistical control group was reached, however.

Because this Report necessarily reports on the approved protocol and statistical plan, it makes reference to use of the CREST study as a historical control and the original 95% effectiveness rate. The 95% effectiveness rate target appears to be a moot point, as the data currently support a 99.8% effectiveness rate; however, the statistical plan attached is the one approved under the IDE, so it still references the 95% effectiveness rate target.

We provide this background to let the Agency know that we acknowledge the lack of binding agreement on the above two items, and to clarify that this Report necessarily contains and reflects the original IDE approved documents (protocol, statistical plan), since there are no other approved documents to report against.

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C. Study Design/Endpoints

The Pivotal Trial of the Essure System (formerly known as STOP) was designed as a multi-center, non-randomized, single-arm, international study of women seeking permanent contraception. The study was conducted in the U.S., Europe, and Australia. The targeted study population was 400 women in whom bilateral Micro-insert placement was achieved. It was expected that more than 400 women would need to be enrolled in order to obtain 400 women in whom bilateral placement was achieved.

The primary endpoints for this study were:

- Prevention of pregnancy;
- Safety of the Micro-insert placement procedure; and
- Safety of the Micro-insert wearing.

The secondary endpoints for this study were as follows:

- Participant satisfaction with the Micro-insert placement procedure;
- Participant satisfaction with Micro-insert wearing;
- Bilateral Micro-insert placement rate; and
- Development of a profile for an appropriate candidate for the Essure procedure.

The study was designed to include 5 years of post-alternative contraception follow-up, 1 year of which was to be completed prior to a PMA filing. The remaining 4 years will be completed as part of post-market surveillance. Binding agreement to file the PMA based on one-year follow-up of 400 women has been reached (see letter from FDA dated August 2, 2001, **Exhibit A**). Subsequent to the binding agreement, FDA accepted our proposal to file the PMA with one-year follow-up visits completed on 350 women (see FDA letter dated March 15, 2002, **Exhibit A**).

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It should be noted that the study had two phases: 1) the “Post-Device (Micro-insert) placement” (PDP) phase, and 2) the “Post-Alternative Contraception” (PAC) phase. The “Post-Device Placement” phase was the time period between Micro-insert placement and the 3-month visit, during which women were instructed to rely on alternative contraception. At the 3-month visit, a hysterosalpingogram (HSG) was conducted to evaluate Micro-insert location and tubal occlusion. Assuming both were satisfactory, women were instructed to discontinue alternative contraception, thus entering the “Post-Alternative Contraception” (PAC) phase of the study, during which they relied on Essure solely for contraception. If the HSG was not satisfactory, then, depending on the circumstances, women were instructed to either seek alternative contraception or remain in the “Post-Device Placement” (PDP) phase until a second HSG or Micro-insert placement procedure was performed.

D. Clinical Trial Conduct/GCP Compliance Statement

The study was conducted in compliance with Good Clinical Practices (GCPs) – 21 CFR, Parts 50, 54, 56 and 812. All sites conducted the study according to the same protocol as that approved by the FDA (IDE # G000055) and by the Medical Device Authority (MDA) in the United Kingdom. All sites also obtained approval from an Institutional Review Board (IRB)/Ethics Committee (EC) before study commencement.

(b) (4)



E. Clinical Trial Monitoring

(b) (4)



8

(b) (4)



F. Study Population/Selection Criteria (Inclusion/Exclusion)

Study women were those seeking permanent contraception. Permanent contraception candidates were screened for eligibility to participate in this clinical study. Candidates who met the inclusion and exclusion criteria and who were willing to participate in the study were provided with an Informed Consent form for their review and signature prior to screening tests.

The objectives of the inclusion and exclusion criteria were to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

The detailed inclusion and exclusion criteria are provided in the protocol, **Volume 3, Exhibit A.**

30

G. Control Population

(b) (4)



²⁶ See Appendix A to February 3, 2000 submission in follow-up to Pre-IDE meeting, as well as Section X of the original IDE application, and Appendix E of August 7, 2000 response to 2nd conditional approval letter.

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H. Investigational Sites

(b) (4)



I. Number of Investigators/Number of Subjects per Investigator

(b) (4)



33

Table 1. Investigators/# Women Scheduled for Micro-insert Placement Procedure

Location	Investigator	Site number	No. Women
(b) (4), (b) (6)			

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34

J. Clinical Protocol

The complete protocol is provided in **Volume 3, Exhibit A**. The Informed Consent form for the study is provided in **Volume 3, Exhibit B**. The Patient Questionnaires and the electronic Case Report Forms for the study are provided in **Volume 4²⁷**. A flowchart of the study sequence can be found below in **Figure 1**, followed by a brief summary of each protocol visit.

(b) (4)



Eligibility

The eligibility phase, through screening questions, counseling, and physical exam and labs, was designed to:

- Ensure prior fertility
- Maximize current fecundity
- Minimize chance of regret
- Minimize confounding issues with long-term Micro-insert wearing
- Minimize potential for poor protocol compliance

Screening

(b) (4)



Micro-insert Placement

Day of procedure activities were to:

- Conduct a pregnancy test, pre-procedure
- Review counseling, pre-procedure
- Perform the Micro-insert placement procedure
- Conduct the pain assessment and satisfaction questions post-procedure
- Conduct the X-ray verification of Micro-insert placement
- Provide post-procedure instructions, covering patient diaries/questionnaires and need for alternative contraception

(b) (4)



37

(b) (4)



38

(b) (4)



39

K. Study Period

(b) (4)



²⁸ Some women had second device placement procedures that occurred beyond this date. All such procedures occurred by June 2001.

40

L. Investigational Device Accountability

The Investigational device accountability information is provided in **Exhibit B**.
All study devices were accounted for.

M. Statistical Methods

(b) (4)



N. Patient Tree

(b) (4)



(b) (4)



4

O. Withdrawn/"Safety Only" Women

(b) (4)



(b) (4)



P. Patient Demographics

(b) (4)



(b) (4)



49

(b) (4)



Q. Study Deviations

(b) (4)



57

R. Study Results

(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



57

(b) (4)



(b) (4)



59

(b) (4)



³⁵ See second conditional approval letter dated June 21, 2000, item #34.

60

(b) (4)



(b) (4)



62

(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



67

(b) (4)



60

(b) (4)



(b) (4)



(b) (4)



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(b) (4)



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(b) (4)



(b) (4)



(b) (4)



(b) (4)



(b) (4)



77

(b) (4)



(b) (4)



9

(b) (4)



80

(b) (4)



(b) (4)



(b) (4)



(b) (4)



84.

(b) (4)



85

(b) (4)



86

5. Reliance on Essure

(b) (4)



(b) (4)



(b) (4)



(b) (4)



91

(b) (4)



92

(b) (4)



73

(b) (4)



94

(b) (4)



95

(b) (4)



96

Table 45. Adverse Events Preventing Reliance

(b) (4)



97

(b) (4)



98

(b) (4)



99

7. **Effectiveness**

(b) (4)



100

(b) (4)



101

(b) (4)



102

(b) (4)



(b) (4)



104

(b) (4)



105

(b) (4)



(b) (4)



Censoring

(b) (4)



107

(b) (4)



108

S. Justification for Use of Foreign Data

(b) (4)



109

T. Conclusions Drawn from the Study

(b) (4)



110

(b) (4)



(b) (4)



112

(b) (4)



113

U. Risk to Benefit Analysis

(b) (4)



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(b) (4)



115

(b) (4)



116

(b) (4)



117

(b) (4)



118

V. Case Report Forms for Lost to Follow-up Participants

Case Report Forms for lost-to-follow-up women are included in **Volumes 5-7**.

W. Summary Data Tables

Summary data tables for the data freeze as of April 2, 2002 are included in **Volume 8-10**. Since the data freeze on April 2, several tables have had minor corrections made to the data within the (b) (4) due to errors noted on the tables. The correct data is reflected in the actual study results and the data tables included with the June 10, 2002 update on 400 women will reflect the corrections.

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Exhibit A - FDA Correspondence
Binding Agreement (FDA Letter August 2, 2001)
Early PMA Acceptance (FDA Letter March 15, 2002)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAR 15 2002

(b) (6)

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1021 Howard Avenue
SAN CARLOS CA 94070

Re: M010031 Early Submission of PMA Application for Essure System
Received: December 21, 2001
Amended: February 13, 2002

Dear (b) (6) :

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To summarize, here is what would be required to go to the July panel meeting:

- April 30, 2002 -- Initial submission of original PMA, with 350 subjects from pivotal study with at least 1-year contraceptive follow up *and* 193 subjects from the Phase II study with 1-year follow up, including 100 subjects with 2-year follow up.
- June 10, 2002 – Major PMA amendment with update of 1-year follow up data, at least 400 subjects and full statistical analysis.
- July 22-23, 2002 – FDA would take the PMA to panel, acknowledging that the clinical data set does not contain 1-year follow up on all subjects enrolled in the pivotal study.

If you have any questions, please call (b) (6)

(b) (6)

Sincerely yours,

(b) (6)

Center for Devices and Radiological Health



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

RECEIVED
AUG 10 2001
BY: _____

AUG 2 2001



Conceptus, Inc.
1021 Howard Avenue
San Carlos, California 94070

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The STOP™ Device is a tubal occlusive device intended to effect female sterilization by occlusion of the fallopian tubes. The STOP™ System consists of STOP™ Device and the wire used for the device placement. The Device is made of an inner coil platinum wire; an outer coil made of nitinol "ribbon" and polyester fibers between the outer coil windings. The design is a straight inner coil of platinum wire with an outer coiled ribbon, attached to the delivery wire with solder on the guide wire. It is designed so when clockwise torque is applied, the device is disengaged from the delivery wire, and the outer platinum coil engages into the epithelial wall of the fallopian tube anchoring the device in the tube.

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If you have any comments or questions regarding this letter, please contact

(b) (6)



Sincerely yours,

(b) (6)



Center for Devices and
Radiological Health

Enclosure

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Minutes of Meeting

Participants:

CDRH/FDA

Conceptus, Inc.

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Date: June 29, 2001

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(b) (4)



Prepared by: (b) (6) – 7/12/01

Revised: 7/17/01, 7/20/01, 7/23/01, 7/26/01, 7/30/01

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Exhibit B - Investigational Device Accountability

Exhibit B - Investigational Device Accountability

Devices were either hand carried by Conceptus personnel or were shipped via courier just in time for clinical cases. Device accountability logs accompanied device shipments. Sites completed the logs and returned all unused product to Conceptus. Two types of Essure Systems were sent: 1) multi-piece systems that required on site assembly, and 2) one-piece pre-assembled systems that were used right from the package. The change from the multi-piece unassembled system to the one-piece pre-assembled system was reported to the FDA in a 5-day notification⁴⁷. **Tables 1 and 2** summarize the device accountability for each configuration. All devices were accounted for and no devices were left at Investigational Sites.

Table 1. Investigational Device Log: Multi-Piece* Unassembled Design

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⁴⁷ 5-day notification dated October 27, 2000; G000055/S8.

Table 2. Investigational Device Log: One-Piece* Pre-assembled Design

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Exhibit C - Study Deviations

Exhibit D - Luteal Phase Pregnancies

Exhibit D - Luteal Phase Pregnancies

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⁴⁸ Wilcox AJ, Baird DD, Dunson D, et. al. Natural limits of pregnancy testing in relation to the expected menstrual period. JAMA Vol 286 No. 14, Oct 10, 2001.

⁴⁹ Peterson HB, et.al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol 1996; 174:1161-70.

⁵⁰ The CREST data was collected at a time when early pregnancy testing was not available. Thus, women who did not have an advancing pregnancy were likely never diagnosed if they had early pregnancy loss. Whereas in our study, women were diagnosed very early and in fact one pregnancy was also spontaneously resolving at the time of diagnosis.

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Exhibit E - Predictors of Placement Failure

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⁵¹ A woman could have had any of the above outcomes, so the number excluded in the analysis was not the sum of the figures presented.

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Exhibit F – Learning Curve Analysis

**Exhibit G – Histology Picture from Perforated Micro-insert
(b) (6) removed from peritoneal cavity**

Exhibit H – Censoring Analysis for Effectiveness Calculation

Exhibit I - Country-by-Country Analysis of Placement, Adverse Event and Reliance Rates

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PO20014/03/C1
APR 22 2002

APR 22 2002

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Volume 3

Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

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**A Multi-Center Clinical Trial to Demonstrate the Safety and
Effectiveness of the STOP Device in Providing Permanent
Contraception**

**Conceptus Research Protocol
STOP 2000**

**Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070
U.S.A.**

Telephone: (b) (6)

Fax: (650) 610-8363

REVISION HISTORY

Original Protocol, Rev 00	02/28/2000
Revision 01	05/18/2000
Revision 02	09/11/2000

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1. TITLE

“A Multi Center Clinical Trial to Demonstrate the Safety and Effectiveness of the STOP Device in Providing Permanent Contraception.”

2. PURPOSE OF STUDY

The purpose of this study is to demonstrate the safety and effectiveness of the STOP device in providing permanent contraception.

3. STUDY DESIGN

The study in approximately 10-20 study sites will be a multi-center, international study of participants who are seeking permanent contraception. The study population will consist of 400 participants in whom bilateral device placement is achieved. It is expected that more than 400 participants will need to be enrolled in order to obtain 400 participants in whom bilateral placement is achieved. A maximum of 500 participants will be enrolled for STOP device placement.

Findings from the U.S. Collaborative Review of Sterilization (CREST¹ study) will be used as a historical control.

Reference

1. Peterson HB, Xia Z, Hughes JM, et al. The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-1170

4. STUDY PLAN

In order to assure a reasonable distribution of participants across sites, Investigators will be requested to enroll a minimum of 10 participants for device placement. Each site will also be restricted to a maximum enrollment of 100 participants so that no more than 20% (100/500 participants) of the study data are enrolled at one site. In addition, each site will be restricted to enrolling no more than 33% of study participants between ages 34-40. Enrollment will be completed when the last site has enrolled at least 10 participants within the specified age criteria.

It is anticipated that the investigational sites will be located in the United States, Europe, and Australia. All sites will conduct the study according to the same protocol and will obtain approval from an Institutional Review Board (IRB) or

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Ethics Committee (EC) before study commencement. Additionally, all sites will be monitored according to the same standard operating procedures (SOPs) in accordance with U.S. Good Clinical Practice (GCP) medical device regulations, the informed consent provisions of the Declaration of Helsinki, and the European Standard EN540: Clinical Investigations of Medical Devices for Human Subjects.

5. PRIMARY AND SECONDARY ENDPOINTS

5.1 The primary endpoints for the study are as follows:

1. Prevention of pregnancy,
2. Safety of device placement procedure, and
3. Safety of device wearing.

Pregnancy prevention will be determined by a pregnancy test at the one year follow-up visit (15 months post-placement), representing 12 months of effectiveness data, since participants must rely on alternative contraception during the first 3 months post device-placement. Any pregnancies diagnosed by this time point will be counted as device failures. Pregnancies occurring during the first 3 months will be assumed to be failure to adhere to this aspect of the protocol or a failure of the alternative contraception, and will not be counted as a failure of the STOP device. Safety of the device placement procedure will be evaluated by recording adverse events on the day of the device placement procedure and at the one-week telephone follow-up. Safety of device wearing will be evaluated by recording adverse events at each of the scheduled follow-up visits and by patient diaries.

5.2 The secondary endpoints for the study are as follows:

1. Participant satisfaction with device placement procedure,
2. Participant satisfaction with device wearing,
3. Bilateral device placement rate, and

4. Development of a profile for an appropriate candidate for the STOP procedure.

Participant satisfaction with the device placement procedure and device wearing will be evaluated by a participant questionnaire and participant interviews at scheduled follow-up visits. Bilateral device placement rates will be noted on the Case Report Forms for the device placement procedure. Development of a profile for an appropriate candidate for the STOP procedure will be achieved by analyzing the data on both successful and failed device placement cases as well as screening failures to ascertain any potential common traits. Screening failures are defined in section 9.1.2 of this protocol.

6. INVESTIGATORS AND QUALIFICATIONS

Investigators selected to participate in this study are gynecologists with extensive experience in hysteroscopy and, preferably, tubal cannulation. Investigators will complete a training program including the following: 1) a review of the protocol requirements, informed consent procedures, and placement theory; 2) practice on a hysteroscopic simulator; 3) device placement technique conducted in perihysterectomy participants; and 4) interpretation of device placement by hysteroscopy, HSG and pelvic x-ray. Initial device placements in hysterectomy participants will be proctored by a previously trained investigator. Each new investigator will be certified by the proctoring investigator when the didactic and clinical training has been completed. Investigators will also have an adequate participant population and clinical research staff to support the study objectives and timelines.

7. STUDY POPULATION

Study participants will be women who are seeking permanent contraception. Prior to taking part in the study, the Investigator or his or her designee will fully inform the participant of the potential risks and benefits of study participation, according to the Informed Consent approved by the overseeing IRB / Ethics Committee. The participant will be given the opportunity to discuss fully any questions she may have.

8. INCLUSION AND EXCLUSION CRITERIA

The inclusion and exclusion criteria are listed below.

8.1 Inclusion Criteria

- 8.1.1 Women who are age 21 to 40;
- 8.1.2 Women who are between 90-300 pounds (40-136 kilograms);
- 8.1.3 Women who are seeking permanent contraception;
- 8.1.4 Women who can accept the risk of pregnancy occurring while relying on the STOP device for prevention of pregnancy;
- 8.1.5 Women who have a minimum of 4-8 coital acts per cycle;
- 8.1.6 Women who have had at least one live birth;
- 8.1.7 Women who are in a monogamous relationship and at low risk for sexually transmitted infections;
- 8.1.8 Women who agree to undergo STOP device placement under hysteroscopic control, in an office or ambulatory setting and are willing to accept the risk of unsuccessful placement;
- 8.1.9 Women who are able and willing to use either a barrier method or oral contraceptive pills (combination of estrogen plus progestin containing ≤ 35 mcg of synthetic estrogen or progestin only pills for women who are contraindicated to estrogen), for the first three months following STOP device placement. Acceptable barrier methods include use of a diaphragm, condom or cervical cap with spermicides. Unacceptable methods of alternative contraception include injectible contraceptives (Depo-Provera), contraceptive implants, IUD, withdrawal, rhythm, sponges and spermicide alone;
- 8.1.10 Women who are willing to keep a coital/menstrual log for 6 months following the device placement procedure;

- 8.1.11 Women with regular, cyclical menses (with a cycle length of 21-35 days) the 2 months prior to the device placement procedure;
- 8.1.12 Women who can be available for all study visits;
- 8.1.13 Women who are able to understand the risks and benefits of participating in the study and are willing to provide signed informed consent; and
- 8.1.14 Women who have the mental capacity to comply with the protocol requirements and provide reliable feedback regarding device wearing.

8.2 Exclusion Criteria

- 8.2.1 Women who are medically contraindicated to pregnancy;
- 8.2.2 Women who delivered a baby or terminated a second trimester pregnancy less than six weeks before the STOP device placement procedure;
- 8.2.3 Women who are unsure about their desire to end their fertility;
- 8.2.4 Women who refuse to use the required alternative contraception (barrier method or oral contraceptive as specified in Inclusion Criteria 8.1.9) for the first three months following device placement;
- 8.2.5 Women with a known abnormal uterine cavity or fallopian tubes that makes visualization of, or access to, the ostia difficult;
- 8.2.6 Women with known cervical or uterine neoplasia or its precursors;
- 8.2.7 Women with untreated acute cervicitis;
- 8.2.8 Women with unexplained abnormal uterine bleeding or intermenstrual bleeding within two months prior to the device placement;

8.2.9 Women who have not had at least two regular menses after the following gynecological events:

8.2.9.1 childbirth, miscarriage or termination of pregnancy

8.2.9.2 Depo-Provera injection

8.2.9.3 irregular periods treated with oral contraceptives which have since been discontinued

8.2.9.4 removal of implants (i.e., levonorgestrel- and desogestrel-containing implants);

8.2.10 Women who had irregular menses prior to or during IUD use and have not had two regular menses since IUD removal;

8.2.11 Women with a history of chronic pelvic pain, severe dysmenorrhea, or severe dyspareunia;

8.2.12 Women who have had one or both fallopian tubes removed or ligated;

8.2.13 Women who have had tubal reanastomosis for the purpose of becoming pregnant or surgery to repair the fallopian tubes;

8.2.14 Women with a prior history of ectopic pregnancy;

8.2.15 Women with known unresolved tubal, ovarian or endometrial pathology;

8.2.16 Women diagnosed with postpartum endometritis or infection from an abortion in the last 3 months;

8.2.17 Women currently diagnosed with acute pelvic inflammatory disease or a history of pelvic inflammatory disease without subsequent pregnancy;

8.2.18 Women with a prior history of infertility treatment;

8.2.19 Women for whom surgery is contraindicated;

8.2.20 Women with a known allergy to contrast media;

8.2.21 Women with current autoimmune or rheumatologic disorders;

8.2.22 Women who have hypertension or diabetes that is not controlled by medications; and

8.2.23 Women who are experiencing chronic pain or have been treated for chronic pain in the last 12 months.

8.3 Withdrawal Criteria:

Study participants may withdraw from the study at any time. The Investigator will discuss with the participant any medical follow up that may be required.

9. STUDY PROCEDURES

Study procedures are summarized in Appendix A, Schedule of Events. All study procedures will be paid for by the Sponsor.

9.1 Participant Eligibility and Screening

9.1.1 Eligibility

Permanent contraception candidates will be screened for eligibility to participate in this clinical study. Candidates who meet the inclusion and exclusion criteria and who are willing to participate in the study will be provided with an Informed Consent for their review and signature prior to screening tests. Candidates will be given ample time to consider their decision to enroll in the study.

9.1.2 Screening

9.1.2.1 Women who have read and signed the Informed Consent Form will be interviewed for demographic and socioeconomic data. These data are recorded for the purpose of collecting participant history and will not be used to exclude potential participants.

9.1.2.2 The Investigator will take a complete medical history and conduct a routine physical exam. Any remarkable findings will be noted on the case report forms.

9.1.2.3 A pelvic exam and required laboratory tests will be performed. Participants will be tested for the presence of *Neisseria gonorrhoea* and *Chlamydia trachomatis* infections. Additionally, the participant will have a blood test to obtain a hemoglobin and white blood cell count to determine if the participant is anemic or has an infection. These tests must be done no longer than two months prior to the scheduled device placement procedure. If more than two months elapse between these tests and the placement procedure, the tests will be repeated. The participant will also receive a Pap Smear (unless she has had a normal Pap Smear within the last 12 months).

9.1.2.4 Participants will be excluded from the study if they test positive for *Neisseria gonorrhoea* or *Chlamydia trachomatis* infections, have a Pap smear indicating dysplasia or carcinoma, have an abnormal white blood count (<3.5 or $>12.0 \times 10^9/\text{Liters}$) or hemoglobin of < 10 grams/deciliters. If laboratory results are abnormal, participants should be treated as medically indicated. The test(s) in question must be repeated with acceptable results prior to enrollment for device placement.

9.1.3. Alternative Contraception Prior to Device Placement

9.1.3.1. If the participant has been relying on an IUD for contraception and had normal menses prior to and during IUD use, a separate appointment will be scheduled at least one week prior to STOP device placement to remove the IUD. IUD removal should not take place concurrent with STOP device placement. If the participant had abnormal bleeding prior to or during IUD use, then the device placement procedure must be deferred until the participant has at least two normal menses following IUD removal. If

the participant does not return to normal menses after IUD removal, then she will be excluded from the study.

9.1.3.2. If the participant is not routinely using oral contraceptives, but chooses to do so for the required alternative contraception period 3 months following the device placement procedure, then she must start taking the oral contraceptives 5 weeks before the device placement procedure to ensure the efficacy of oral contraceptives.

9.1.3.3. If a women chooses a diaphragm for her contraceptive methods in the first three months after STOP device placement, she should be fitted for the diaphragm during the screening visit.

9.1.4. Participant Scheduling

Whenever possible, device placement will be performed during days 7-14 of the proliferative phase of the menstrual cycle (where day 1 represents the first day of bleeding) in order to enhance visualization of the fallopian tubal ostia.

9.2. STOP Device Receipt and Accountability

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9.3. STOP Device Placement

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9.3.6. Summary of Steps for STOP Device Placement Procedure

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9.4. Management of Cases with Unsuccessful Device Placement

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9.5. Device Removal

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9.6. Participant Diary and Questionnaires

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9.7. Follow-up Visits and Phone Contact

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9.8. One Week Follow-up Phone Contact

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9.9. Three-Month Post-Device Placement Follow-Up Visit

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9.10. Three-, Six-, Eighteen-Month and Three-, Four-Year *Post-Discontinuation of Alternative Contraception*

Follow-Up Phone Contact

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9.11. One-, Two- and Five-Years *Post Discontinuation of Alternative Contraception*

Follow-Up Visit

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10. ADVERSE EVENTS

Adverse events are defined as any untoward deviations in subject health away from baseline. Investigators must record and document all adverse events in the case report form, and record and report any unanticipated device related adverse effects to Conceptus and the reviewing IRB / Ethics Committee as soon as possible but no longer than 5 working days after becoming aware of the event. Unanticipated adverse device effect means any serious adverse effect on health or safety, or any life-threatening problem or death caused by or associated with a device, *if* that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan *or* any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects. For all serious adverse events, the Investigator will send to Conceptus all appropriate paperwork (discharge summaries, office notes, etc.) that might be pertinent.

11. RECORDS AND REPORTS

11.1 Each Investigator will maintain the following accurate, complete and current records relating to the Investigator's participation in an investigation:

11.1.1 All correspondence with another Investigator, an IRB or Ethics Committee, the sponsor, a monitor, or the FDA / other health authority, including required reports.

11.1.2 Records of receipt, use or disposition of the STOP device.
(Please refer to maintenance of the Investigator Device Log described in section 9.2.1.)

11.1.3 Records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

11.1.3.1 Documents evidencing informed consent.

11.1.3.2 All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

11.1.3.3 A record of the exposure of each subject to the STOP device, including the date and time of each use, and any other therapy.

11.1.4 The protocol, with documents showing the dates of any reasons for any deviation from the protocol.

11.1.5 Any records that FDA or other health authority requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

11.2 The Investigator or designee will input the required study data into password protected, electronic case report forms that will be maintained on a website. Further instructions regarding access to the website and use of the electronic case report forms will be provided during site training.

- 11.2.1 Paper print-outs of the completed case report forms will be kept in the Investigator's facilities. Case Report Forms should be printed out after Conceptus monitoring and data queries have been completed for the specified form. Forms (both electronic and paper) will be accessible to the Investigator, his or her authorized staff, and to representatives of the Sponsor for the purpose of monitoring the study and auditing the data and participant records. The United States Food and Drug Administration (FDA) or other health authority also may require access to the forms and participant records.
- 11.2.2 Participant identity will be kept confidential by assigning unique participant numbers to each participant. The medical record number for each participant will be recorded on a participant number log in order to allow traceability of each participant's records. Participant numbers and initials will be used to identify participants on case report forms. Participant names will not be kept with the data. Any publications or presentations that result from this study will maintain participant confidentiality.
- 11.3 Each Investigator shall prepare and submit the following complete, accurate and timely reports:
- 11.3.1 Unanticipated adverse device effects (please refer to section 10 of this protocol for reporting requirements).
- 11.3.2 Withdrawal of IRB or Ethics Committee approval. An Investigator shall report to Conceptus, within 5 working days, a withdrawal of approval by the reviewing IRB/Ethics Committee of the Investigator's part of an investigation.
- 11.3.3 An Investigator shall submit progress reports on the investigation to Conceptus, the monitor, and the reviewing IRB or Ethics Committee at regular intervals, but in no event less often than yearly.

- 11.3.4 Deviations from the investigational plan. An Investigator shall notify Conceptus and the reviewing IRB or Ethics Committee of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by Conceptus is required for changes in or deviations from the protocol, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, approval from the FDA or other health authority and the IRB/Ethics Committee also is required.
- 11.3.5 Informed consent. If an Investigator uses a device without obtaining informed consent, the Investigator shall report such use to Conceptus and the reviewing IRB or Ethics Committee within 5 working days after the use occurs.
- 11.3.6 An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB or Ethics Committee.
- 11.3.7 An Investigator shall, upon request by a reviewing IRB or Ethics Committee, FDA or other health authority, provide accurate, complete and current information about any aspect of the investigation.
- 11.4 Each Investigator will maintain all study-related records during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a pre-market approval application (PMA) or a notice of completion of a product development protocol.

12. ANALYSIS AND REPORTING OF RESULTS

- 12.1 Throughout the study, data will be compiled and analyzed by Conceptus. When appropriate, data will be made available to Investigators for publishing and presentation purposes. Conceptus has the right of final approval prior to data presentation or submission for publication.
- 12.2. The data will be summarized in a tabular format, with means, standard deviations and 95% confidence intervals and sample size. A Bayesian approach will be used for the primary outcomes. Such an approach for other outcomes will be considered. A more detailed statistical plan can be provided upon request.

13. ETHICAL CONSIDERATIONS

Eligible study candidates will be women who are seeking permanent contraception. Candidates will be fully informed of the assumed irreversibility of the study procedure, and the risks and potential benefits associated with the procedure. The participant should be allowed ample time between the giving of consent and undergoing the study procedure to consider her decision and to ask questions. Additionally, participants must be willing to accept the risk that pregnancy could occur while relying on the STOP device for prevention of pregnancy.

13.1 Risks

Following are the potential risks, precautions and benefits associated with the study.

13.1.1 There is a risk of pregnancy and ectopic pregnancy and risks associated with the treatment for both. If the participant conceives and chooses to continue an intrauterine pregnancy, she will be informed that the risks of the device to the participant, to the fetus and to the continuation of the pregnancy are unknown.

13.1.1.1 In women who have become pregnant with an IUD in place, 41% have a miscarriage in the first and early second trimester and the rest carry pregnancy to term. One

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percent of the pregnancies carried to term with an IUD in place have resulted in stillbirth. Therefore, if the participant elects to continue a pregnancy with the STOP devices in place, there is a high likelihood of miscarriage and a low likelihood of stillbirth.

13.1.1.2 Any participant who becomes pregnant while wearing the STOP device will be followed through her pregnancy or termination. All risks and complications encountered during the pregnancy, delivery or termination will be recorded.

13.1.2 Risks Associated with the Device Placement Procedure

13.1.2.1 Local anesthesia, oral analgesia/sedation, regional anesthesia (i.e., spinal, epidural), oral or conscious (intravenous) sedation, or general anesthesia may be administered to the participant to prevent or reduce the participant's discomfort. The associated risks will be covered and administered by the anesthesia informed consent from the institution or clinic at which device placement will take place. Regardless of the type of anesthesia, participants may not be able to resume all normal activities for 12-24 hours following the procedure.

13.1.2.2 Pain, cramping and vaginal bleeding may occur during and following the device placement procedure. Typically, these incidents are tolerable, transient and successfully treated with medication.

13.1.2.3 During and/or directly following the device placement procedure, there is the risk that study participants will experience nausea or vomiting. This is expected to be transient and may be treated with medication as required.

13.1.2.4 A small percentage of participants may experience fainting on the day of the procedure.

13.1.2.5 Perforation or dissection of the fallopian tube or uterine cornua has been reported in less than 5% of Phase II cases conducted with the STOP device. Bleeding and scarring may result from such a perforation or dissection; however, treatment is typically not required.

13.1.2.6 There is a risk of uterine perforation by the hysteroscope or other instruments used during the procedure with possible injury to the bowel, bladder, and major blood vessels. Surgical intervention may be required, but is unlikely, if such injury were to occur. To reduce the risk of uterine perforation, the procedure will be terminated if excessive force is required to achieve cervical dilatation.

13.1.2.7 There is a risk that the STOP device may be inadvertently placed into the myometrium of the uterus and not into the fallopian tube lumen. If one device has already been properly placed in one fallopian tube, in addition to inadvertent placement into the myometrium, the Investigator may place a third device to complete the procedure. If bilateral placement is not achieved, this may result in the participant having one device in the fallopian tube and/or one device in the myometrium that cannot be relied upon for contraception. Placement of the device in the myometrium may result in post-operative pain which may be successfully treated with medication. If surgical removal of the device(s) is required, this may require salpingectomy or hysterectomy.

13.1.2.8 There is a risk that the STOP device may be placed too distal in the fallopian tube. If removal of the device is necessary, surgery will be required.

13.1.2.9 There is a risk that the STOP device may perforate through the tubal wall or uterine cornua which could result in the device being released into the peritoneal cavity. Post-operative pain and/or menstrual disturbance may be experienced and may be successfully treated with medication. If the participant elects to undergo incisional sterilization, device retrieval may be attempted if the Investigator believes it is safe to do so. However, device retrieval may not be possible if the device cannot be visualized by the Investigator.

13.1.2.10 There is a risk that STOP device placement will only be achieved in one fallopian tube. If this occurs, study participants may be left with one device *in vivo* that cannot be relied upon for permanent contraception.

13.1.2.11 There is a risk that STOP placement will not be possible in either fallopian tube. Participants will be counseled regarding alternative methods of permanent contraception.

13.1.2.12 There is a minimal risk of fluid absorption of the physiologic saline fluid used for distention of the uterus to perform the hysteroscopic procedure. However, this is expected to be a remote risk due to: 1) the short time necessary for the device placement procedure; and 2) no resection, laceration or other disturbance of the endometrium is intended. If excess fluid absorption occurs, the body should eliminate the fluid through sweat and urine.

13.1.2.13 As with all invasive procedures, the device placement procedure can cause an infection. An infection could cause damage to the uterus, fallopian tubes, or pelvic cavity. This could require antibiotic therapy, hospitalization, or surgery, including hysterectomy.

13.1.3 Risks Associated with STOP Device Wearing

13.1.3.1 There is a risk that the STOP device could move out of the fallopian tubes. This movement could be expulsion (movement out of the fallopian tube and into the uterine cavity/cervix/vagina or out of the body) or migration (movement to the distal fallopian tube or out of the fallopian tube and into the peritoneal cavity). Additional x-rays may be required to identify the location of the device(s), and surgery may be required to remove the device(s). Device movement could result in pregnancy, ectopic pregnancy and/or pain/ menstrual disturbance.

13.1.3.2 As with currently available methods of mechanical permanent contraception (i.e., clips, rings), if the STOP device is to be removed, surgery will be required. Further, it is possible that surgical removal of the fallopian tubes (salpingectomy) and uterus (hysterectomy) may be required.

13.1.3.3 Abdominal/pelvic pain and cramping may occur. Pain and cramping may be a more likely occurrence during the menstrual period, during and after sexual intercourse or other physical activity.

13.1.3.4 Intermenstrual bleeding or heavier than normal bleeding may be experienced.

13.1.3.5 A positive emotional side effect for most women who have a permanent contraception procedure is a feeling of freedom from the fear of pregnancy. Sometimes, a woman is mildly depressed for a short time; this is normal. Occasionally, a woman may regret her decision to undergo permanent contraception.

13.1.4 Risks Associated with Follow-up Procedures

13.1.4.1 A minimum of four pelvic x-rays and one hysterosalpingogram are required over the five-year duration of this protocol. During any x-ray procedure there is exposure to radiation. On average, there are .0005 rads in a pelvic x-ray. This is less than the radiation exposure from a transcontinental flight. There are approximately .033 rads in the fluoroscopic portion (<30 seconds) of a hystero-salpingogram procedure. As a point of comparison, radiation exposure from a barium enema is 0.85 rads which is higher than the HSG required by this protocol.

13.1.4.2 The use of contrast media, used to perform the HSG, has been associated with allergic reaction in some participants undergoing cardiovascular radiological procedures. Allergic reaction can result in hives or difficulty breathing. In some individuals, an anaphylactic response may occur which can lead to death.

13.1.4.3 The following risks are additionally associated with the HSG procedure; vasovagal response; infection, which may require antibiotic treatment and in rare cases could require hospitalization; intravasation; perforation of the uterus; uterine cramping and/or bleeding; pain or discomfort; and allergic reaction to latex. Latex has been reported to be associated with anaphylactic reactions in rare cases.

13.1.5 Risks Associated with Potential Future Procedures

13.1.5.1 Participants who undergo placement of the STOP device may, in future years, be offered intrauterine therapies that utilize electrical energy. It is recommended that electrocautery be avoided in surgical procedures undertaken on the uterine cornua and fallopian tubes. All other procedures in the pelvis should avoid the use of

electrocautery within 4cm of the device. Due to the presence of the STOP devices, there may be risks associated with such procedures that, at this time have not been identified.

13.1.5.2 Any intrauterine procedure such as endometrial biopsy, D&C, hysteroscopy (diagnostic or operative) including endometrial ablation could interrupt the ability of the devices to prevent pregnancy. In addition, the presence of the STOP devices could entail risks associated with such procedures that, at this time, cannot be quantified.

13.1.5.3 Participants may decide, in future years, to undergo in vitro fertilization (IVF) to become pregnant. The effects of the STOP devices on the success of IVF are unknown. If pregnancy is achieved, the risks of the device to the participant, to the fetus and to the continuation of a pregnancy are unknown.

13.1.6 As with any experimental device, there is the potential that unknown risks exist.

If the participant experiences a complication, her progress will be followed until it has resolved or is not expected to change.

13.2 Potential Benefits

There is a possible benefit to the participant if the STOP device is found to be safe and effective in preventing pregnancy. Since the STOP device is placed using a non-incisional technique without general anesthesia, it is possible that the STOP device placement procedure may be less painful, less risky, less costly, and/or require a shorter period of recovery than incisional methods of sterilization that are currently used. Also, the STOP device procedure will not leave an abdominal scar. Finally, since participants are awake during the procedure, they may experience less anxiety and a greater sense of control.

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14. FINANCIAL ISSUES

(b) (4)



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15. DATE OF COMMENCEMENT

The proposed date of commencement for this clinical trial is May 2000. It is estimated that the study enrollment at sites will be completed approximately 6-9 months from the date the study starts. Study participants will be followed for five years following discontinuation of alternative contraception.

16. MANUFACTURING

All STOP devices will be manufactured by Conceptus Inc. in San Carlos, California, USA.

17. INVESTIGATOR'S SIGNATURE

The Investigator will be required to sign the following statement, after reviewing the protocol.

I have carefully read and I understand the provisions of this protocol, and I agree to follow it in every detail. Furthermore, I understand that any changes to the protocol must be pre-approved by the Sponsor and the reviewing Ethics Committee or Institutional Review Board. I agree not to release to any third party, either during or after the study, any information about the STOP device, or about the study. All data for this study will be provided to the Sponsor and remains the sole property of the Sponsor. I agree that any presentation or publication of study data will be pre-approved by the Sponsor. I affirm that all study participant records will be stored safely and kept confidential, and will only be used for the purpose for which it has been approved.

INVESTIGATOR'S PRINTED NAME

INVESTIGATOR'S SIGNATURE

DATE

Appendix A

Schedule of Events

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(b) (4)



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CONFIDENTIAL

Pivotal Trial Protocol: STOP 2000
Dated: September 11, 2000

Appendix B

Protocol for Management of Potential Device Movement or Unsatisfactory Device Location

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P020014/V4/C1

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PMA
Conceptus, Inc.

Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

Table of Contents for Pivotal Trial

Volume 4

Exhibit A - Patient Questionnaires

Exhibit B - Electronic Case Report Forms

P020014/V5/C1

ADR 22 2002

Table of
Contents for
Volume 5

PMA
Conceptus, Inc.

Conceptus Essure™ System

Pre-Market Approval Application

(PMA)

Table of Contents for Pivotal Trial

Volume 5

Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

P020014 / 06 / CA

APR 22 2002

Table of
Contents for
Volume 6

Conceptus Essure™ System

Pre-Market Approval Application

(PMA)

Table of Contents for Pivotal Trial

Volume 6

Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

Patient (b) (6) [REDACTED]

Patient (b) (6) [REDACTED]

Patient (b) (6) [REDACTED]

Patient (b) (6) [REDACTED]

Patient (b) (6) [REDACTED]

P020014/V7/C1

APR 22 2002

Table of
Contents for
Volume 7

PMA
Conceptus, Inc.

Conceptus Essure™ System

Pre-Market Approval Application

(PMA)

Table of Contents for Pivotal Trial

Volume 7

Exhibit A - Case Report Forms for Lost-to-Follow-up Participants

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

Patient (b) (6)

P020014/08/01

APR 22 2002

Table of
Contents for
Volume 8

Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

Table of Contents for Pivotal Trial

Volume 8

Summary Data Tables:

- Number 1 -** Patient Enrollment and Reasons for Discontinuation
- Number 2 -** Months of Wearing
- Number 3 -** Months of Effectiveness
- Number 4 -** Demographics and Baseline Characteristics
- Number 5 -** Device Placement Procedure
- Number 6 -** Anesthesia

P020014/v9/c1

APR 22 2002

Table of
Contents for
Volume 9

Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

Table of Contents for Pivotal Trial

Volume 9

Summary Data Tables:

- Number 7 -** Post-procedure Pain and Recovery
- Number 8 -** Adverse Event on Day of Placement
- Number 9 -** Follow-up HSG Results
- Number 10 -** One-week Phone Contact
- Number 11 -** Days of Work Missed
- Number 12 -** Daily Pain Assessment Questions
- Number 13 -** One-week Phone Contact Adverse Events

P020014/V10/C4

APR 22 2002

Table of
Contents for
Volume 10

Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

Table of Contents for Pivotal Trial

Volume 10

Summary Data Tables:

- Number 14** - Three Month PDP Office Visit
- Number 15** - 3-month HSG Results
- Number 16** - 3 Month Follow Up Adverse Event
- Number 17** - 3 Month PAC Phone Contact
- Number 18** - Diary data
- Number 19** - 6 Month PAC Phone Contact
- Number 20** - One-year PAC Office Visit
- Number 21** - One-year PAC Office Visit - Adverse Event
- Number 22** - Subjects Able to Rely on Device

P020014/VII

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APR 22 2002



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ACOG Technical Bulletin #222 – April 1996

Sterilization

Over 170 million couples worldwide use surgical **sterilization** as a safe and reliable method of contraception. In the United States, **sterilization** is the most commonly used method among married or formerly married women. An estimated 640,000 female **sterilization** procedures and 500,000 male **sterilization** procedures are performed each year (1, 2). In 1988, **sterilizations** accounted for 39% of contraceptive method use by all women 15-44 years old; 27.5% of women using contraception had undergone tubal **sterilization**, and 11.7% reported that their partners had undergone vasectomy (3).

Patient Counseling and Selection

Patients should be informed about both male and female **sterilization** as well as the risks and benefits of alternative long-acting, temporary contraceptive methods (see the box). When appropriate, the male partner can be included in such initial counseling. Many men and women have the impression that **sterilization** operations are easily reversible. The clinician should make clear to the patient that all operative **sterilizations** are intended to be permanent. Counseling should take into account risk factors that affect regret of **sterilization**. In the United States, the strongest indicator of future regret is young age at the time of **sterilization**, regardless of parity or marital status. Women between the ages of 20 and 24 years at **sterilization** are twice as likely to experience poststerilization regret as women **sterilized** between the ages of 30 and 34 years (4). Marital instability increases the probability of regret. Approximately 6% of **sterilized** women report regret or request information about **sterilization** reversal within 5 years of the procedure; urologists estimate that close to 1-2% of the total number of men they **sterilize** seek information on vasectomy reversal (4, 5). Although success rates in vas and tubal reanastomosis have improved dramatically in recent years, successful reversal and subsequent pregnancy depend on many factors, including the type of **sterilization**, interval between **sterilization** and reversal, age, and length of the remaining tube.

Preoperative counseling should include an explanation of the causes and probability of **sterilization** failure. When the patient has considered and accepted the risks of regret or failure, the physician can provide information about operative approaches, including a review of the possible complications from both the operation and the anesthesia. The patient should be informed about the advantages and disadvantages of local and general anesthesia, pain likely to be associated with the operation, and possible complications, including damage to organs or major vessels, infection, and subsequent ectopic pregnancy. The patient should be informed of her need for adequate postoperative care and support, and she should plan accordingly.

The patient should be given an opportunity to ask questions about the procedure. Both this discussion and the fact that the patient was given the opportunity to ask questions should be noted in the patient's record by the physician. All this is best accomplished at a preoperative visit scheduled far enough in advance of the operation to allow the patient ample time to weigh the factors involved in the decision. Physicians should be aware of state laws or insurance regulations that may require a specific interval between obtaining consent and performance of **sterilization** procedures. State law may mandate the use of special consent forms. Written informed consent should be obtained following counseling in a relaxed and unpressured environment. It is best not to obtain consent concurrent with labor or an abortion procedure because these events are associated with stress and a high incidence of regret of **sterilization**.

Components of Presterilization Counseling

Alternative methods available, including male **sterilization**

Reasons for choosing **sterilization**

Screening for risk indicators for regret

Details of the procedure, including anesthesia with attendant risks and benefits

The permanent nature of the procedure and information on reversal

The possibility of failure, including ectopic pregnancy

Post tubal ligation physiology, including the possibility of unrelated change in menstruation

The need to use condoms for protection against sexually transmitted diseases and human immunodeficiency virus infection if at risk of exposure

Answers to all questions to the satisfaction of the patient

Completion of informed consent document

Modified from Pritlock AH, Soderstrom DM. Permanent sterilization. In: Gerson EL, Demian EJ, Tyrer LB, eds. Family control. 2nd ed. London, Ontario: Baldey Publishers; 1994:223-236.

Patients should be advised that female and male **sterilization** offer no protection against sexually transmitted diseases (STDs) such as human immunodeficiency virus (HIV) infection. Patients should be encouraged to use condoms or have their partners use condoms when they are at risk of exposure. In the United States, studies indicate that **sterilized** women with risk factors for STDs have low rates of condom use and infrequently attend clinics for preventive reproductive health services (6, 7).

Tubal Sterilization

Timing

Tubal **sterilization** can be performed postpartum, postabortion, or as an interval procedure (unrelated in time to a pregnancy). The timing of the procedure will influence both the surgical approach and the method of tubal occlusion used.

Postpartum **sterilizations** are performed at the time of cesarean delivery while the abdomen is open or following a vaginal delivery using a 2-5-cm subumbilical minilaparotomy incision. The subumbilical minilaparotomy approach allows for easy entry into the abdomen and access to the tubes because the anterior abdominal wall is thin just below the umbilicus over the fundus. It is best to perform postpartum minilaparotomy before the onset of significant uterine involution but following full assessment of maternal and neonatal well being. The likelihood of postpartum hemorrhage in multiparous women subsides after the first 12 hours postpartum. Postpartum minilaparotomy may be performed safely and comfortably using local anesthesia with sedation or regional or general anesthesia.

Postabortion **sterilizations** can be performed safely following uncomplicated spontaneous or induced abortion. Following a first- trimester abortion, laparoscopic **sterilization** or minilaparotomy using a suprapubic approach are both acceptable. In either case, a single anesthetic for the abortion and the **sterilization** may be used to avoid additional risk. Following a second-trimester abortion, minilaparotomy via a small midline vertical incision at the level of the fundus can be used safely. Open laparoscopy or the Hasson cannula may be used, thereby avoiding the risk of perforation of the soft, enlarged uterus associated with introduction of the laparoscopic trocar. Alternatively, an interval procedure can be performed once complete uterine involution has occurred.

Tubal **sterilization** can be performed as an interval procedure at any time during the menstrual cycle. Although performance of the **sterilization** procedure during the patient's estimated follicular phase and confirmation of patient use of a highly effective method of contraception before **sterilization** will reduce the risk of luteal phase pregnancy (a pregnancy diagnosed after **sterilization** in which conception occurred before **sterilization**), highly sensitive pregnancy testing will further reduce the risk. A same- day presterilization urine test capable of detecting human chorionic gonadotropin levels as low as 20 mIU/ml or a qualitative serum assay for the beta subunit of human chorionic gonadotropin will suffice (8). Tests this sensitive will allow for pregnancy detection as early as 1 week after conception. Performance of dilation and curettage concurrent with all interval **sterilizations** as a routine practice is not recommended on the basis of effectiveness, cost, and morbidity (9). Interval **sterilization** is usually performed using laparoscopy or minilaparotomy with local, regional, or general anesthesia. Transvaginal approaches have been described, and transcervical hysteroscopic approaches are being investigated.

Surgical Approach

Laparoscopy

Modern laparoscopy was first developed in Europe in the 1960s and became a popular method for direct visualization of the abdominal and pelvic organs. In the 1970s, it was introduced in the United States for tubal **sterilization**. In 1987, approximately one third of all tubal **sterilizations** in the United States were laparoscopic procedures. Most of these were performed under short-acting, general anesthesia in an outpatient setting.

In the United States, closed laparoscopy is used more often than open laparoscopy. In laparoscopic-**sterilization**, an endoscope is inserted through a small incision made just below the umbilicus. Closed laparoscopy is performed through a small subumbilical skin incision just large enough to admit a sharp trocar. The trocar is used to puncture the abdominal wall, gaining entry into the peritoneal cavity blindly. Open laparoscopy is performed through a 1.5-cm semilunar or vertical subumbilical incision made through the

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layers of the abdominal wall until the peritoneal cavity has been entered under direct visualization (10).

Advantages of laparoscopy over other surgical approaches for **sterilization** include the opportunity to inspect the abdominal and pelvic organs, barely visible incision scars, and a rapid return to full activity for the patient. The disadvantages of laparoscopic **sterilization** include the cost and the fragility of the equipment, the special training required, and the risk of bowel, bladder, or major vessel injury following insertion of the needle or trocar.

With special training and experience, both closed and open laparoscopy can be performed with local anesthesia while maintaining a high level of patient comfort. Small studies have indicated that many women prefer the use of local anesthesia for **sterilization** procedures (11).

Minilaparotomy

The minilaparotomy approach may be performed by using local anesthesia with sedation, regional anesthesia, or general anesthesia. In contrast to laparoscopy, minilaparotomy requires only basic surgical instruments and training. Minilaparotomy is performed by using a 2-3-cm incision placed in relation to the uterine fundus. For interval **sterilization**, a uterine manipulator may be used to bring the uterine fundus toward the incision. For women undergoing either laparoscopic or minilaparotomy procedures with local anesthesia, placement of a paracervical block before insertion of the uterine manipulator reduces discomfort (12). Although most surgeons prefer to perform tubal occlusion using suture ligation and excision techniques, clips or rings may be applied through the minilaparotomy incision. With minilaparotomy, a segment of the tube can be removed for pathologic confirmation that both tubes were **sterilized**.

Methods of Occlusion

Electrocoagulation

Electrocoagulation for tubal occlusion is used exclusively with laparoscopic **sterilization**. Unipolar electrocoagulation with or without tubal excision was the first laparoscopic method of tubal occlusion. However, because uncommon but serious complications, including thermal bowel injury, were reported, bipolar coagulation was introduced and is now the most commonly used laparoscopic method in the United States. Bipolar coagulation also results in a more localized injury to the fallopian tube than does the unipolar method. Therefore, to maximize its effectiveness, at least 3 cm of the isthmic portion of the fallopian tube must be completely coagulated. Adequate coagulation requires sufficient energy of 25 W delivered in a cutting waveform (13). Use of a current meter, rather than a visual endpoint or a defined period of time, more accurately indicates complete coagulation.

Mechanical Methods

Mechanical occlusion devices commonly used in the United States include the silicone rubber band (Falope ring) and the spring-loaded clip (Hulka-Clemens clip). A new titanium clip lined with silicone rubber (Filshie clip) has been widely used in Great Britain with low reported failure rates (14, 15).

Special applicators are necessary for each of the mechanical occlusive devices, and each requires skill for proper application. The band can only be applied to a fallopian tube that is sufficiently mobile to allow it to be drawn into the applicator. Both types of clips should be applied perpendicular to the long axis of the proximal isthmus of the fallopian tube. Both types of clips and the silicone rubber band are most likely to be effective when used to occlude a normal tube. Tubal adhesions or a thickened or dilated fallopian tube increase the risk of misapplication and subsequent failure (16).

All of the mechanical methods of tubal occlusion destroy much less oviduct (about 5 mm for clips and 2 cm for rings) than do electrocoagulation methods. Therefore, if reversal is attempted, there is a greater chance of success.

Ligation Methods

Tubal occlusion at the time of cesarean delivery, laparotomy for other indications, or minilaparotomy is usually performed by using ligation techniques. A variety of techniques have been well described (17). Care should be taken to excise a sufficient section of fallopian tube to ensure complete transection of the tubal

lumen.

Efficacy

Failure

Precise failure rates for each method of tubal occlusion and long-term cumulative failure rates have been difficult to measure because of the methods' high effectiveness rates. A generally accepted failure rate of less than 1% is based on combined small studies in which different occlusion methods were used (18). Preliminary findings from the U.S. Collaborative Review of **Sterilization** indicate that cumulative failure rates are higher than expected, with significant differences between methods (19). The risk of failure persists for years after the procedure and varies by method of tubal occlusion and age. In a total of 143 **sterilization** failures, cumulative 10-year probabilities of pregnancy were highest after spring-loaded clip **sterilization** (36.5 per 1,000 procedures) and lowest after unipolar coagulation (7.5 per 1,000) and postpartum partial salpingectomy (7.5 per 1,000). The cumulative risk of pregnancy was highest among women **sterilized** at a young age with bipolar coagulation (54.3 per 1,000) and spring-loaded clip application (52.1 per 1,000). It is important to note, however, that in another study of **sterilization** failures, all spring-loaded clip failures were found to be due to misapplication (16).

Fecundity declines significantly after the age of 35 years. In one study, patients younger than 35 years were 1.7 times more likely to become pregnant following **sterilization** than women over the age of 35 years (20). In another study, among women 18-27 years of age who underwent bipolar coagulation, 2.8% became pregnant between 5 and 10 years after the procedure (19).

Pregnancies after **sterilization** may occur without any technical error. Technical error leading to failure occurs less frequently with minilaparotomy regardless of the occlusion method used (21). In one study, the location of the suture on the ligated tube affected estimated minilaparotomy failure rates, which were approximately 3% in 3 years for fimbriectomy with infundibular ligation, approximately 1.7% for ampullary ligation, and approximately 0.34% for isthmic ligation (20).

Ectopic Pregnancy

When **sterilization** failure occurs, the subsequent pregnancy is more likely to be ectopic than intrauterine. The degree of increased risk depends on the occlusion method used. The results of several reports suggest that over half of the pregnancies that occur after electrocoagulation **sterilization** procedures may be ectopic (22, 23). If an ectopic pregnancy occurs, the physician should evaluate both proximal tubes and manage any acute problems that are present.

Complications

In the United States, female **sterilization** has a mortality rate of 1-2 deaths per 100,000 procedures (24). Complications of general anesthesia are the leading cause of death from tubal **sterilization**. Other causes include sepsis and hemorrhage. Between 1977 and 1981, most of those deaths from sepsis resulted from thermal bowel injury following unipolar electrocoagulation, while most of those deaths from hemorrhage followed major vessel lacerations associated with abdominal entry for laparoscopic **sterilization** (25).

Studies in the United States indicate that women undergoing interval minilaparotomy are at approximately twice the risk of having any complication than are women undergoing interval laparoscopic **sterilization**. However, women who undergo minilaparotomy often have medical risk factors, including certain cardiac and pulmonary problems, that are contraindications to laparoscopy and therefore are intrinsically at greater surgical risk (26, 27).

Late Sequelae

The long-term health effects of tubal **sterilization** on menstrual pattern disturbance, pelvic pain, and the need for pelvic surgery are controversial. Early studies of menstrual disturbance following **sterilization** failed to account for confounding variables such as presterilization use of hormonal contraceptives that generally mask underlying menstrual dysfunction. Most recent prospective studies that account for these factors have found little or no difference in menstrual function between women before and after **sterilization**, or between **sterilized** women and nonsterilized control subjects in the first 2 years of follow up. Findings from reports

that include follow up for more than 2 years have been less consistent, yet no single method of occlusion, regardless of the amount of tubal destruction, has been associated with an increase in risk for poststerilization menstrual disturbance (28).

Two studies have evaluated the likelihood of hospitalization for menstrual disorders in women who have undergone **sterilization**. A U.S. population-based cohort study showed an increased relative risk of 1.6 (95% confidence interval of 1.3-2.1) for hospitalization for menstrual disorders compared with a control group of wives of men who have had vasectomies (29). Follow up of a large British cohort for 6 years failed to identify a significant increase in risk (30).

Some **sterilized** women may be more likely to undergo subsequent hysterectomy. Women who have been **sterilized** before age 30 have a higher risk of a hysterectomy than women **sterilized** after age 30. This risk has not been related to an increase in menstrual disturbance or the extent of tissue damage based on the method of occlusion used (31).

Ovarian Cancer

In several older studies, an inverse relationship between tubal occlusion and subsequent ovarian cancer has been found, although the strength of this relationship has varied widely (32, 33, 34). A controlled, prospective study reported a reduced risk of ovarian cancer among women who had tubal occlusion or hysterectomy (35). The study monitored 77,544 women for 12 years. For those women who had a tubal ligation, the relative risk of ovarian cancer was 0.33. The reduced risk persisted after the investigators controlled for risk factors such as smoking and protective factors (eg, use of oral contraceptives). Cases of reported ovarian cancer, identified within the first 4 years after **sterilization**, were excluded to eliminate possible screening bias (32, 33).

Pelvic Inflammatory Disease

It has long been believed that tubal **sterilization** protects against pelvic inflammatory disease. This would seem to make intuitive sense, as this condition is thought to be caused by the ascent of bacteria through the cervix, uterus, and fallopian tubes and into the peritoneal cavity. This protection is, however, not absolute. Case reports of pelvic inflammatory disease and tuboovarian abscess in women who have undergone **sterilization** are rare but do exist in the literature (36, 37).

Sterilization in Men

Vasectomy performed as an outpatient procedure has been popular in the United States since 1965. More than 5 million men in the United States have had a vasectomy (38). When compared with tubal **sterilization**, vasectomy is safer, less expensive, and equally as effective. In the United States, urologists, general surgeons, and family physicians perform vasectomy procedures in their offices using local anesthesia.

Traditionally, vasectomy was performed through two incisions in the scrotum, one overlying each vas deferens. The incisions were then closed with a suture. In 1985, the no-scalpel vasectomy technique was introduced (39). This method makes use of two specially designed instruments: one allows the vas to be fixed externally, while the second is used to puncture the scrotal skin without using a scalpel (40). The technique was developed to increase acceptability of vasectomy by reducing the apprehension related to making an incision on the scrotum (41, 40). It reduces the already low rate of minor complications (less than 3%) seen with traditional vasectomy, such as wound hematoma and infection (42).

Both traditional and no-scalpel vasectomy use the same methods to occlude the vas. These include excising a segment of the vas and sealing the ends via ligation, electrocoagulation or thermocoagulation, or clips. To decrease the incidence of recanalization, some surgeons further separate the severed ends by folding them back on one another or burying one end in the scrotal fascia.

Pregnancy rates following vasectomy are less than 1% in most studies and usually result from failure to occlude the correct structure, unprotected intercourse too soon after the operation, or spontaneous recanalization. Unlike tubal occlusion in women, vasectomy is not immediately effective: about 3 months or 20 ejaculations are needed to flush the vasa of viable sperm. Postvasectomy semen analysis should be performed to determine the effectiveness of the procedure.

The possibility of long-term side effects from vasectomy has received considerable attention. Nine separate

epidemiological studies in men have failed to show a relationship between atherosclerosis and vasectomy (43). An original study in monkeys that suggested such a relationship has not been confirmed (44, 45). Other consequences of vasectomy have been suggested, but none has been proven. In addition, several studies report that in the United States, men who have chosen vasectomies are often healthier than control counterparts (46, 47).

In Western countries, white, upper-middle-class men are more likely to choose vasectomy and are also the group more likely to have testicular cancer. A study of nearly 74,000 men who have had vasectomies showed the incidence of testicular cancer in this group to be no higher than that of the general population (48). It also showed that vasectomy does not accelerate the growth of preexisting testicular tumors.

In 1993, researchers published the first large cohort studies to show a weak but statistically significant increased risk for prostate cancer in a subgroup of men at least 20 years after vasectomy (49, 47). Two subsequent studies have failed to support these findings (50, 51).

The U.S. National Institutes of Health convened a group of experts in 1993 to review the published reports on prostate cancer. The committee found that although additional research into a possible causal relationship between vasectomy and prostate cancer should be conducted, a change in the current practice of vasectomy was not warranted. The National Institutes of Health made the following recommendations (52):

- Providers should continue to offer vasectomy and perform the procedure
- Vasectomy reversal is not warranted to prevent prostate cancer
- Screening for prostate cancer should not be any different for men who have had a vasectomy than for those who have not

Summary

Sterilization provides a safe and effective contraceptive method. Both female and male **sterilization** have few long-term sequelae. Several new methods of transcervical **sterilization** are under development, but laparoscopy and minilaparotomy are likely to remain the most popular methods of female **sterilization**.

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Issues in Brief

Family Planning Improves Child Survival and Health

Babies who survive and children who enjoy good health are universal humanitarian goals. Strategies to advance these goals in developing countries include both direct investments in health and nutrition programs and the increased availability of family planning services. These two strategies complement each other, and should be viewed together. Especially in times of fiscal austerity and reduced international assistance, they should not be pitted against each other in competition for scarce funds.

The basic conditions necessary for newborns to survive and for children to flourish are no secret. The ideal would be for all babies to be born to mothers who are in good health, who have obtained adequate prenatal care and who have access to the health facilities necessary for a safe delivery. Also needed are sufficient breastfeeding, good nutrition after weaning, hygienic living conditions—especially clean water and modern sanitation—and medical care that includes immunization against childhood diseases.

But two other, related factors also contribute to improved child health and survival in developing countries. These are smaller families and the use of methods of contraception that allow couples to plan their families. When women can plan when and how many children to have, the number of "high-risk" pregnancies and births is reduced, and infant and child health and survival improve.

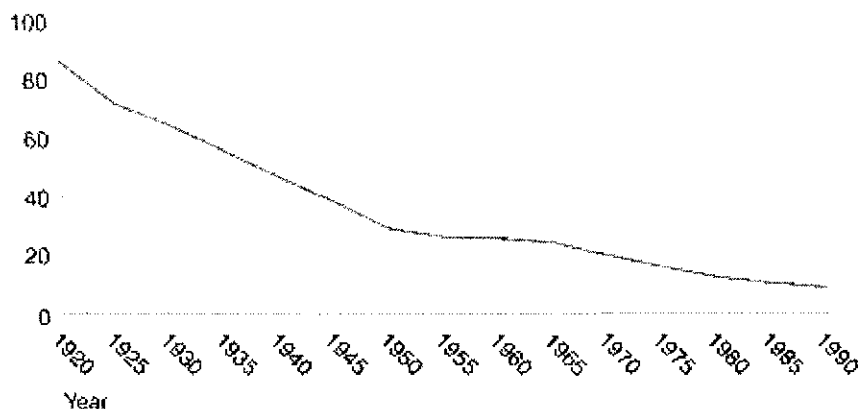
Because the conditions that enhance babies' health and chances of survival can be found in most of the developed world, the high infant mortality rates of the past have largely disappeared in the West. In France, Japan and the United States, for example, fewer than 10 babies die for every 1,000 live births. Thus, for most Americans, the death of a baby is a rare event.

Yet some older Americans can remember when infant deaths were as common in the United States as they are currently in many parts of the developing world (Chart A). In 1920, the U.S. infant mortality rate was as high as Nigeria's is today (87 infant deaths for every 1,000 live births; Table 1, column 1). In 1965, it still equaled the current rate of 25 deaths per 1,000 in Sri Lanka, and in inner-city communities particularly, the rate remains close to that level.

chart a
U.S. Infant Mortality

In the 1920s, one of every 20 babies died before their first birthday; in the 1990s, fewer than one in 100 do so.

Infant deaths per 1,000 live births



Source: National Center for Health Statistics, Vital Statistics of the United States, 1991: Vol. II—Mortality, Part A, U.S. Government Printing Office, Washington, D.C., 1996

table 1
Influencing Infant Survival

Country and year	Infant mortality rate	% of births less than 24 months apart	% of births unplanned	If want no more births, % not using effective method
Sub-Saharan Africa				
Botswana, 1988	38	6	53	65
Burkina Faso, 1992–1993	94	9	24	92
Burundi, 1987	74	9	24	97
Cameroon, 1991	64	6	20	84
Cen. Afr. Rep., 1994–1995	97	11	23	92
Cote d'Ivoire, 1994	89	7	28	93
Ghana, 1993	66	5	43	86
Kenya, 1993	62	13	51	62
Liberia, 1986	144	10	u	86
Madagascar, 1992	93	16	23	90
Malawi, 1992	135	11	41	85
Mali, 1987	105	9	14	98

Namibia, 1992	57	7	33	49
Niger, 1992	123	15	13	95
Nigeria, 1990	87	8	11	89
Rwanda, 1992	85	13	49	81
Senegal, 1992– 1993	68	11	28	90
Tanzania, 1991– 1992	92	6	22	85
Togo, 1988	77	6	39	95
Uganda, 1996	81	8	28	87
Zambia, 1992	107	6	32	83
Zimbabwe, 1994	53	5	42	57
North Africa, Middle East				
Egypt, 1992	62	12	34	45
Morocco, 1992	57	10	33	56
Sudan, 1989– 1990	70	10	23	90
Tunisia, 1988	48	16	32	49
Asia				
Bangladesh, 1993–1994	87	6	32	51
India, 1992– 1993	79	10	23	61
Indonesia, 1994	57	6	17	41
Pakistan, 1990– 1991	86	20	21	81
Philippines, 1993	34	14	44	68
Sri Lanka, 1987	25	14	36	45
Thailand, 1987	35	12	31	26
Turkey, 1993	53	11	31	61
Latin America & the Caribbean				
Bolivia, 1993– 1994	75	11	54	84
Brazil, 1996	39	10	47	27
Colombia, 1995	28	11	45	42
Dominican Republic, 1991	43	16	38	33
Ecuador, 1987	57	14	35	58
El Salvador, 1985	67	7	49	40
Guatemala, 1987	73	12	26	67
Mexico, 1987	47	14	51	45

Paraguay, 1990	34	12	23	58
Peru, 1991–1992	55	11	56	66
Trinidad & Tobago, 1987	28	16	35	53

Notes: u=unavailable. Most data for columns 1–3 refer to all births in the five years before the survey. However, data on birthspacing for about one-third of countries are for 10 years before the survey. In addition, data on unplanned births for Burundi, Namibia, Uganda, Sudan and Mexico refer only to the last birth in the previous five years. Source: All data are from the Demographic and Health Surveys.

We have known for some time that better timing and spacing of pregnancies improves child health and survival. Large-scale studies in Western Europe and North America, published in the late 1970s and early 1980s, confirmed the beneficial effects that planned and timely childbearing have on child survival.¹ More recent evidence from developing countries also compellingly links improved child survival with smaller family size and well-timed pregnancies.²

This Issues in Brief will show how family planning can lead to significant improvements in the survival of newborns and the health of small children. Because women who use contraceptive methods can choose when to become pregnant, they are better prepared than women whose pregnancies are unexpected to seek care for themselves during pregnancy, and able to time their pregnancies to achieve the best situation for the infant.

High-Risk Pregnancies

Pregnancies may have a high risk of a poor or tragic outcome if they occur shortly after a birth, are among very young mothers or women past their childbearing prime, or are among women who have already had many births.³ In addition, high-risk pregnancies increase the mother's risk of dying in childbirth, and when the mother dies, her newborn's risk of dying during its first year of life is also increased.

The ways in which ill-timed pregnancies raise the mortality risks for babies are not fully understood. Most experts agree that the causes are primarily biological, even though social factors also play a role. A mother's age, the number of births she has already had and the spacing of those births all affect her health and her ability to carry a subsequent pregnancy safely to term.

Many high-risk pregnancies end in the birth of premature or very low birth weight babies, and such infants often fail to thrive, or lack the resilience needed to overcome the many threats to survival they may face during the first days and months of life. The early weaning that occurs if a mother quickly becomes pregnant again exposes the still-fragile infant to a number of infectious organisms through its intake of water and food rather than breastmilk.

In some instances, newborns face more than one risk-enhancing situation: Some older women giving birth have already had several children; some women with large families have had many pregnancies in rapid succession; and some adolescent mothers not only are physically immature, but are giving birth for the second or third time.

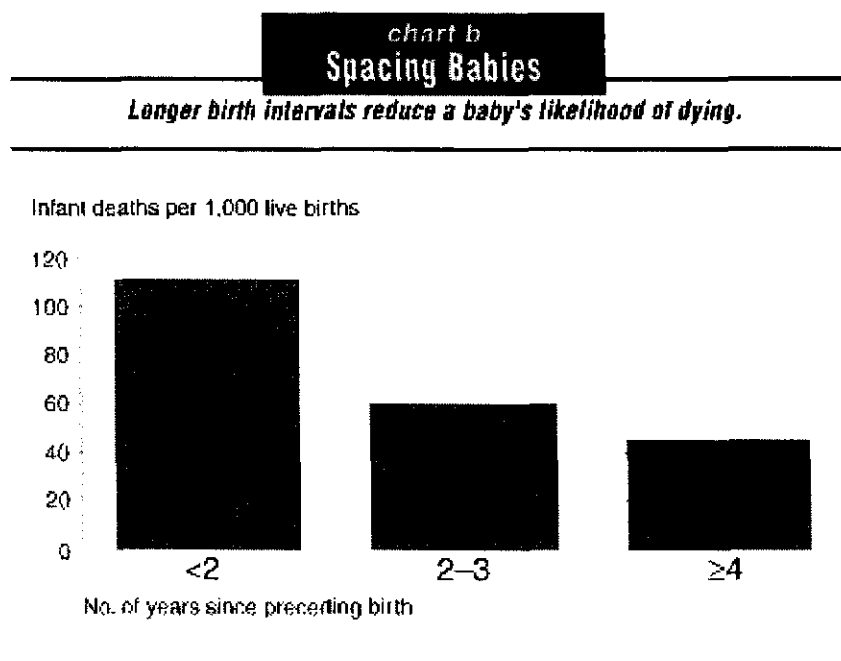
In addition, many women in the developing world whose pregnancies are high-risk for

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biological reasons also are at risk for social and economic reasons. They often are impoverished, and many live in unsanitary housing, are malnourished and have little education. And many women receive little or no medical care during pregnancy or when they give birth. For these reasons, disentangling the complex web of biological, social, economic and demographic factors that influence rates of child survival is difficult.

Closely Spaced Births

Babies born less than two years apart are much more likely to die than those born after a longer interval, as Chart B shows. This is a serious problem in developing countries where a substantial minority of births occur within less than 24 months of a previous one. Column 2 of Table 1 indicates that closely spaced births account for one in five of all births in Pakistan; one in six in the Dominican Republic, Madagascar, Niger, Tunisia, and Trinidad and Tobago; one in seven in Ecuador, Kenya, Mexico, the Philippines, Rwanda and Sri Lanka; and around one in 10 in another 16 of the 45 developing countries listed.



Source: see reference 2; averages are based on 45 *Demographic and Health Surveys*..

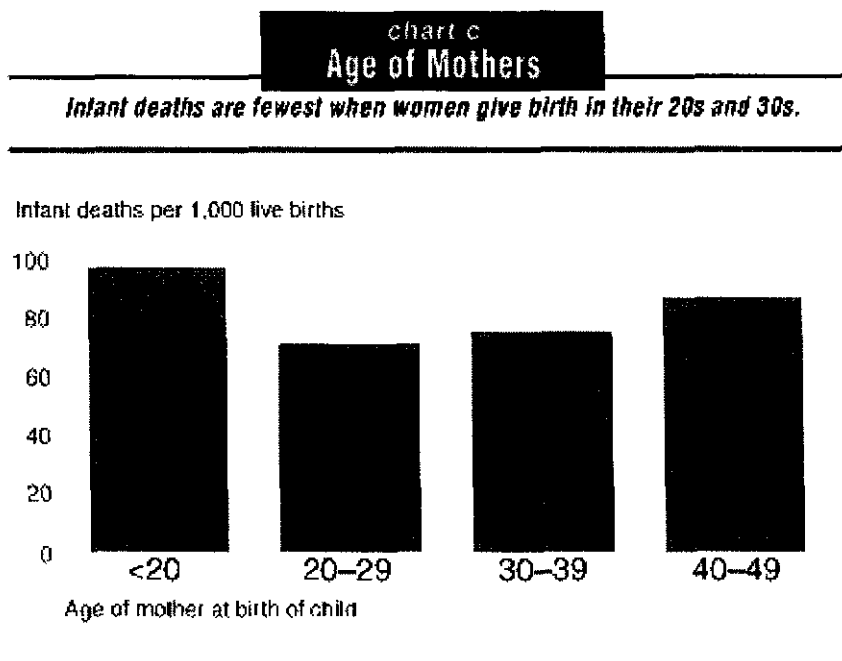
Closely spaced births present a risk to the health of all three family members involved: the mother herself, who does not have sufficient time to regain her strength after delivery; the initial child, who often has to be weaned early; and the baby born subsequently, who is likely to be premature or low-birth-weight. If all births occurring within less than two years of each other could be more widely spaced, one in four infant deaths in developing countries might be prevented.⁴

Some traditional childbearing practices have helped to ensure lengthy intervals between births. In a number of societies, for example, women have breastfed for long durations. At the same time, cultural taboos often require a lactating woman to abstain from sexual relations. Both sexual abstinence and the lengthy duration of breastfeeding have served to lengthen the interval between successive pregnancies. But as these practices become less common than in the past, the incidence of closely spaced births is likely to increase.

As populations everywhere become more urbanized, as commercial infant formulas become more accessible and as women of childbearing age work away from the home in increasing numbers, both the average length of time babies are breastfed and the once common practice of sexual abstinence after a recent birth are declining in many countries. If women who stop breastfeeding and resume sexual relations do not immediately start to practice some form of contraception, they will soon be at risk of becoming pregnant again.

Age of Mothers

Throughout the developing world, babies born to women younger than 20 are, on average, one-third more likely to die than infants born to women in their 20s and 30s (see Chart C). This is mostly because babies born to very young mothers are more likely to be premature, to be low-birth-weight and to suffer from complications at the time of delivery. And many adolescents do not know how to obtain or cannot afford good prenatal and delivery care. In addition, teenage births are likely to be first births, and first births always carry a higher risk than subsequent births.



Source: G.T. Bicego and O.B. Ahmad, 1996 (reference 2), Chart B; averages are based on 40 Demographic and Health Surveys.

The link between early childbearing and lower rates of infant survival in developing countries has serious implications. One in five women aged 20-24 report having had their first child before their 18th birthday, and two out of five report doing so before they were 20.⁵ This high incidence of teenage childbearing is partly because even when adolescents want to prevent pregnancy, they often face special problems in obtaining the contraceptive products or services that would enable them to do so.

In addition, babies born to women older than 40 are at somewhat greater risk of dying in infancy than those whose mothers are in their 20s and 30s. To compound the problem, older women often have several children already, and babies born after the mother has already had a number of children are also more likely to die in infancy than babies whose mother has had only one or two previous births. Further, in the developing world, many older women with

large families are in poor health: They often suffer from such problems as anemia, poor nutrition, cardiovascular disease or uterine prolapse.

For these reasons, helping older women avoid unwanted pregnancy improves child survival. Indeed, high levels of contraceptive sterilization in Latin America (mostly among women in their 30s or older who have had all the children they want⁶) is likely to be one reason for the overall lower infant death rates in Latin America compared with those of Asia and Sub-Saharan Africa (Table 1).

Unplanned Pregnancies

Many women in developing countries acknowledge—even after a new baby is born and part of the family—that they did not plan to have that child. The proportion of births that are reported as unplanned ranges from one-quarter to one-half in most countries (Table 1, column 3). This is troubling because there is some evidence—although it is mostly based on the experience of developed countries—of a link between whether parents wanted a child and its survival and well-being.⁷

In developed countries, women who plan to become pregnant and want a child tend to recognize that they are pregnant soon after conception. Partly because of this earlier awareness, they visit a doctor sooner and generally take better care of themselves during pregnancy than women with unwanted pregnancies. Women with wanted pregnancies are also likely to receive more consideration, support and care from family members. A review by the U.S. Institute of Medicine of the research on this topic concluded that "the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development."⁸

In developing countries, there is less evidence that a baby's safe delivery and healthy growth is linked to whether the pregnancy was a wanted one. In addition, prenatal, maternal and child health services are often not widely available or are of poor quality, and poverty sharply limits how well a family can take care of infants and children who are in poor health.

Yet there is little reason to believe that the degree to which a baby is wanted would not have some effect on women's care of themselves during pregnancy and of their newborns subsequently. One study on Indonesia, Korea and the Philippines demonstrates that even after factors such as the parents' education and economic level and the availability of health clinics are taken into consideration, babies are more likely to suffer from acute respiratory infections and severe diarrhea if the pregnancy was unwanted than if it was wanted.⁹

Understanding the Danger

Most women understand the dangers of having children at closely spaced intervals, of having large numbers of children and of having children late in their reproductive years—the three major biological factors associated with high-risk pregnancies.

When married women in developing countries who already have four children are asked if they would like to have more, about eight out of 10 say no; so do half of women with fewer children.¹⁰

Even among women who say they want another child, the vast majority want to delay their

next pregnancy. Their preferred interval between births is 3–5 years in all regions of the world.¹¹ If women were able to achieve the intervals they want between pregnancies, fewer babies would die in infancy.

But many women who say they want to stop having children altogether or to delay their next pregnancy are not using the contraceptive methods that would help them achieve these goals. In the countries of Sub-Saharan Africa, 57–98% of women who want no more children are not using an effective family planning method (Table 1, column 4). Nor are about half of women who want no more children in most countries of Asia and Latin America.

A Crucial Combination

Family planning services that help women avoid high-risk and unwanted pregnancies can contribute to improvements in infant and child health even in the poorest of countries. The impact of family planning is probably greatest when it helps women space births at healthy intervals, avoid having large numbers of children, and prevent unwanted pregnancies, especially in their later childbearing years.

Programs designed to encourage and enable women to avoid giving birth in their teenage years would also reduce infant mortality rates. However, this requires raising the average age at which most women marry or encouraging young women to postpone their first pregnancy—both difficult goals.

Nevertheless, the crucial contribution of social and economic development to better health should not be overlooked. The improved living conditions that contributed to a declining infant death rate in the United States have yet to reach many areas of the world. Millions of families in Africa, Asia and Latin America still lack clean water, decent housing, good medical services and sufficient food—basic elements needed to alleviate the causes from which most infants are dying: diarrhea, respiratory infections, malaria, measles and malnutrition.

If Americans want their tax dollars to go toward programs that would improve child health and survival in developing countries, such programs should focus on improving broad health services and economic conditions, as well as on making family planning services available to women who want and need them.

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Credits

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Title X and the U.S. Family Planning Effort

Although a woman's ability to become pregnant spans almost half her lifetime, American women today typically want only two children—a goal that, for most, is unrealistic without contraception. One of the United States' key public health goals has long been to expand access to contraceptive services to all those who need and want them, with a special emphasis on reaching those traditionally hindered in their attempts to obtain care by income or other factors, such as age or geography. This *Issues in Brief* examines the 30-year record of the nation's voluntary family planning effort, outlining its origins, describing its current structure and funding, and assessing the impact it has had in preventing unintended pregnancies, births and abortions.

Origins of the Program

Studies conducted during the 1960s showed that rates of unwanted childbearing among low-income women were at least twice as high as those among the more affluent—a phenomenon traceable in large part to inequalities in access to family planning services. By the end of the decade, a sizable, bipartisan consensus had emerged favoring government support of voluntary family planning programs as a means of expanding economic development, alleviating poverty, avoiding welfare dependency and improving the health of women and their families.

Even as this consensus was forming, Congress amended a number of federal laws to allow family planning services to be provided under existing programs. In 1965, as part of the "War on Poverty," federal funds were made available for family planning through the Office of Economic Opportunity. In 1967, Title IV-A of the Social Security Act was amended to require state welfare agencies to offer and provide family planning services to women receiving public assistance.

Then, in 1970, with broad bipartisan support, legislation establishing Title X of the Public Health Service Act was signed into law by President Richard Nixon, creating for the first time a comprehensive federal program devoted entirely to the provision of family planning services on a national basis. The new program sought to fulfill the president's promise that "no American woman should be denied access to family planning assistance because of her economic condition."

Public expenditures for family planning grew rapidly in the early 1970s, as the clinics Title X helped to create became established across the country. In 1972,

in recognition of disparities in services across states, Congress amended the Medic-aid statute (Title XIX of the Social Security Act) to mandate inclusion of family planning services in all state Medicaid programs. By the early 1980s, almost \$340 million in federal and state funds was being spent to provide family planning services to five million women at nearly 5,200 service sites.

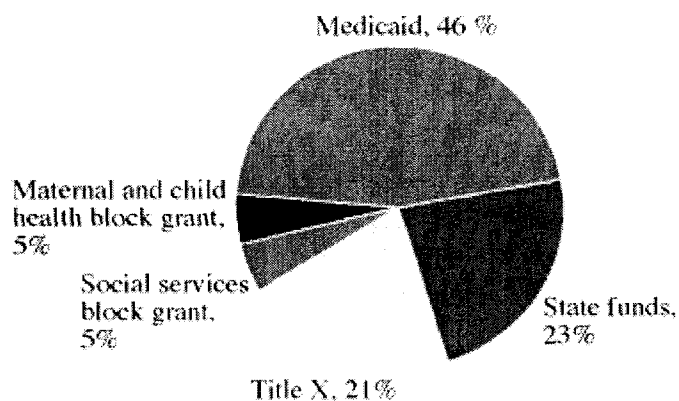
Since then, however, a persistent combination of conservative politics and fiscal pressures has forced family planning clinics to confront both budget cuts and new administrative restrictions. Despite these ongoing struggles, publicly funded agencies continue to provide services to large numbers of low- and moderate-income women and teenagers.

Sources of Funding

Public funds to provide family planning services come from diverse programs with different focuses (see Chart A). The largest source of funding is the federal-state Medicaid program. While nine in 10 family planning agencies derive at least some income from Medicaid reimbursement, few rely heavily on it. Medicaid does not fund family planning clinics or provide services directly. Instead, it is an insurance mechanism whereby federal and state governments reimburse physicians and other health care professionals for the medical services, including family planning, they have provided to eligible individuals.

Chart A: Funding Sources, 1994

Several public programs fund contraceptive services.



Many poor women are not eligible for Medicaid coverage. To qualify in most states, a woman must be single, already have a child (or be pregnant) and have an income below state requirements; nationwide, the average income eligibility ceiling is only about 46% of the federal poverty level, or approximately \$6,100 a year for a family of three.

Most poor and low-income women who do not qualify for Medicaid are dependent on publicly funded clinics for help in obtaining family planning

services. The establishment and operation of these clinics is accomplished through Title X, the only federal program dedicated solely to funding family planning and related reproductive health care services. Clinic services are also partially supported in most states with federal funds from the maternal and child health block grant and the social services block grant (Titles V and XX of the Social Security Act, respectively), but with a few exceptions, family planning services are only a small component of these broad programs.

Finally, state contributions to family planning services have grown considerably since the 1970s; 68% of family planning agencies received some support from state and local sources in 1995. Although 10 states provided no *state* funds for family planning services in 1994, some of these allocated significant proportions of their federal block-grant allotments for this purpose.

Who Provides Services?

In 1994, a total of 3,119 agencies provided organized family planning services—1,413 health departments, 159 Planned Parenthood affiliates, 534 hospitals and 1,013 other types of agencies. Together, these agencies operated 7,122 clinic sites. Of these, 44% were operated by state health departments, 13% by Planned Parenthood affiliates, 11% by hospitals and 32% by other agencies, such as independent family planning councils and community and migrant health centers.

Each clinic site served an average of 923 clients in 1994. Planned Parenthood affiliates reported serving 2,074 clients per clinic, while health department clinics, many of which are located in rural or sparsely populated areas, served an average of 681 clients annually. In the aggregate, however, both types of agencies served about the same proportion of all family planning clinic clients—30% and 32%, respectively.

Who Receives Services?

According to 1994 data, an estimated 6.6 million women receive contraceptive services annually through the network of publicly subsidized family planning providers. Overall, 30% of these clients are younger than 20, 50% are aged 20-29 and 20% are aged 30 or older. A majority of the contraceptive clients served at publicly funded agencies are non-Hispanic whites (61%), while 14% are Hispanics, 19% are blacks and 7% are Asians or of some other race. Most of the clients are poor—57% have family incomes that are below the federal poverty level, and one-third have family incomes of 100-250% of poverty. However, only one-quarter of all clients are Medicaid recipients.

While the reach of the family planning clinic network is encouraging, weaknesses in the provision of services remain. One indicator of the continuing need is shown by a 1995 National Center for Health Statistics report that U.S. women have an average of 3.3 pregnancies over their lifetimes, of which only 1.8 are wanted births. According to the report, white women average 2.8 pregnancies, 1.6 of which are wanted births; black women average 5.1 pregnancies, of which 1.8 are wanted births; and Hispanic women average 4.7

pregnancies, of which 2.6 are wanted births.¹

Services Provided

Family planning agencies provide a variety of contraceptive options—usually at lower cost than available elsewhere—along with the information and education that clients need to choose the best method for their needs. Oral contraceptives are universally available at family planning agencies, but the provision of other methods varies depending upon the type of agency. Planned Parenthood affiliates offer an average of 10 methods, while health departments and community and migrant health centers offer seven contraceptive methods, on average.

Depo-Provera, a hormonal injection that was approved for use in the United States in 1992, is now available from 96% of family planning agencies. Additional methods offered by 90% of agencies include male condoms, spermicides and the diaphragm. Some three-quarters of all agencies also offer natural family planning (periodic abstinence). Norplant is offered by 59% of agencies; the remaining six methods—the IUD, postcoital hormonal pills (emergency contraception), female condom, cervical cap, tubal ligation and vasectomy—are offered by fewer than 50% of agencies.

Besides providing contraceptive methods and related counseling, family planning clinics offer many other reproductive health services. All agencies routinely provide Pap tests, breast and pelvic exams and blood pressure measurement in the course of a woman's contraceptive visit. In addition, the vast majority of agencies provide such services as prenatal, postpartum and well-baby care; immunizations; and services under the Special Supplemental Food Program for Women, Infants and Children (WIC).

It is the policy at 94% of agencies to routinely obtain clients' sexual histories, and three-quarters of agencies routinely test for anemia. Testing for sexually transmitted diseases (STDs), urinary tract infections or pregnancy are routinely provided at some agencies; more often, however, these tests are provided only on indication or if the client requests to be tested. Routine testing for three STDs—gonorrhea, chlamydia and syphilis—is provided by 64%, 54% and 42% of agencies, respectively.

In addition, 96% of agencies routinely counsel clients regarding the risk factors for STDs and the human immunodeficiency virus, and 62% routinely provide education related to condom negotiation skills. All agencies report providing contraceptive education through individual counseling and the distribution of printed materials, and nearly nine in 10 encourage counselors to spend more time with teenagers than with other clients.

The Impact of Services

Publicly funded family planning services have been responsible for preventing large numbers of unintended pregnancies, abortions and births among low-income women, especially unmarried women and teenagers.

- Each year, publicly funded contraceptive services help women avoid 1.3 million unintended pregnancies, which would result in 534,000 births, 632,000 abortions and 165,000 miscarriages.
- In the absence of publicly funded family planning services, the number of abortions performed in the United States each year would be 40% higher than it currently is.
- Without publicly funded family planning services, an additional 386,000 teenagers would become pregnant each year. Of these, 155,000 would give birth, increasing the number of teenage births by one-quarter. Just under 50,000 of these pregnancies would end in miscarriage, and 183,000 teenagers would have abortions, increasing abortions to teenagers by 58%.
- Without publicly funded family planning services, an additional 356,000 women who have never been married would give birth each year, increasing total out-of-wedlock births by one-quarter.
- Of the 534,000 additional women who would give birth in the absence of publicly funded family planning services, 338,000 would be eligible for Medicaid coverage of pregnancy-related care; eight in 10 of these women would be eligible only by virtue of their pregnancy. Therefore, for every public dollar spent to provide family planning services, the public saves an average of \$3 in Medicaid costs for pregnancy-related and newborn care.

The data also show that public funding of family planning services prevents poor birth outcomes and improves women's overall health.

- Publicly funded family planning services increase the likelihood that pregnant women will obtain sufficient prenatal care. A study of 45,000 women who gave birth in North Carolina in 1989-1990 found that women who used family planning services in the two years before conception were more likely to begin prenatal care early and to receive adequate levels of care throughout their pregnancies.²
- A recent national study also found that publicly funded family planning services provided in 1982-1988 prevented 20,000 low-birth-weight deliveries, 6,500 infant deaths and 5,500 neonatal deaths.³
- A recently published analysis of Wisconsin's chlamydia prevention program, which includes family planning clinics as primary screening and treatment sites, found steep declines in the incidence and serious complications of the infection, such as pelvic inflammatory disease and ectopic pregnancy. Between 1987 and 1991, the incidence of new infections in women decreased by 27-50% in clinic populations.⁴

The benefits of publicly funded family planning services in the United States have long been recognized. Authorities in public health have agreed on family planning's effectiveness, not only in preventing unintended pregnancies but also in improving the health of women and children (see box, Family Planning

Benefits, below).

Benefits

- National Commission to Prevent Infant Mortality:
"Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception." *Troubling Trends: The Health of America's Next Generation, 1990*
- March of Dimes Birth Defects Foundation:

"Family planning counseling and services are essential elements of preconception and interconception care. [We] affirm that family planning should be an integral part of perinatal care to improve pregnancy outcome." *Toward Improving the Outcome of Pregnancy: The 90s and Beyond, 1993*
- Institute of Medicine Panel on Adolescent Pregnancy and Childbearing: "The availability of contraceptive services to adolescents depends heavily on public support, in particular funding through Title X, Medicaid and other federal and state maternal and child health programs. In light of the demonstrated effectiveness of contraceptive use in reducing early unintended pregnancy, continued support of these programs is essential." *Risking the Future: Adolescent Sexuality, Pregnancy, and Childbearing, 1987*
- Institute of Medicine Committee on Unintended Pregnancy: "Financial barriers [to contraception] should be reduced by increasing the proportion of all health insurance policies that cover contraceptive services and supplies,...extending Medicaid coverage for all postpartum women...and continuing to provide public funding...for comprehensive contraceptive services, especially for those low-income women and adolescents who face major financial barriers in securing such care. This last point speaks to the major role that public financing programs, such as Title X and Medicaid, have played in helping millions of people secure contraception....It is essential that such public investment be maintained." *The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families, 1995*

The Key Role of Title X

While no longer the largest funder of family planning services, the Title X program continues to be the glue that holds the national family planning system together, largely determining both its structure—through the nationwide network

of clinics—and the substance of services that are provided to low- and moderate-income women and teenagers. In 1994, 4.2 million family planning clients were served by clinics administered by Title X-supported agencies.

Because of the availability of subsidized family planning services, many women do not have to face decisions regarding an unintended pregnancy. In 1994, nearly one million unintended pregnancies were averted among women who attended Title X-funded clinics (see Table 1).

Table 1, Title X Clinics		
State	Clients served (1994)	Pregnancies averted
U.S.	4,156,850	969,700
AL	89,430	20,900
AK	6,690	1,600
AZ	33,330	7,800
AR	73,510	17,100
CA	501,080	116,900
CO	50,630	11,800
CT	49,810	11,600
DE	14,790	3,500
DC	14,540	3,400
FL	168,640	39,300
GA	169,880	39,600
HI	17,480	4,100
ID	29,590	6,900
IL	162,670	37,900
IN	77,750	18,100
IA	74,160	17,300
KS	47,720	11,100
KY	114,470	26,700
LA	58,510	13,600
ME	35,510	8,300
MD	72,210	16,800
MA	70,530	16,500
MI	127,170	29,700
MN	36,520	8,500
MS	78,920	18,400

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MO	93,500	21,800
MT	28,380	6,600
NE	27,110	6,300
NV	17,400	4,100
NH	31,730	7,400
NJ	102,010	23,800
NM	40,170	9,400
NY	237,670	55,400
NC	112,680	26,300
ND	14,250	3,300
OH	141,290	33,000
OK	53,620	12,500
OR	35,130	8,200
PA	262,190	61,200
RI	13,150	3,100
SC	65,810	15,400
SD	17,070	4,000
TN	101,810	23,800
TX	233,300	54,400
UT	15,430	3,600
VT	9,240	2,200
VA	79,130	18,500
WA	88,290	20,600
WV	70,820	16,500
WI	79,050	18,400
WY	11,080	2,600

Title X is administered by the Department of Health and Human Services (DHHS), which is responsible for allocating among the 10 federal health regions the funds appropriated annually by Congress. The federal health administrator in each region receives applications from, and awards grants on a competitive basis to, public agencies and private nonprofit agencies that provide contraceptive services as well as training, technical assistance and other support.

In 1994, a total of 85 primary grantees (1-6 per state) received Title X support. Fifty-one of these were state, territorial, local or municipal health departments; 14 were independent family planning councils (regional, nonprofit umbrella agencies); seven were Planned Parenthood affiliates; and 13 were other types of community agencies, such as hospitals.

Some Title X grantees operate family planning clinics directly, distributing grant funds among their various facilities. Others allocate the money to "delegate

agencies," which operate individual clinics. Agencies providing family planning services, whether primary Title X grantees or their delegates, are diverse, community-based organizations. They include university medical centers, community action organizations, community health centers, nursing service organizations and a wide variety of nonprofit agencies, many of which are located in places where little or no other reproductive health care is available.

In 1994, nearly two-thirds of all women served by family planning clinics, 4.2 million women, obtained care at one of the 4,200 clinics receiving Title X funds. Health department sites were the most likely to receive Title X funding (78%), followed by independent clinics and Planned Parenthood sites (66% each), hospital clinics (28%) and community and migrant health centers (18%). Overall, clinics receiving Title X funds served at least 25% more clients per site than those that did not. In addition, because Title X funding is not tied to specific medical services for specific eligible clients, the agencies that received this funding were able to serve more uninsured, near-poor clients, more adolescents and more members of other special populations than were clinics that did not receive these funds.

Title X also determines the substance of the services offered to individuals. Each grantee is ultimately responsible for ensuring that its delegate agencies and the clinics they run meet the program's requirements. The law establishes a broad definition of family planning and sets standards for reproductive health care with which all providers receiving any Title X funds must comply. The Title X regulations and official program guidelines outline in great detail protocols for the provision of family planning services that comport with nationally recognized medical standards, including a mandate that patients at clinics supported by Title X be offered—on a purely voluntary, confidential basis—the full range of contraceptive methods and related counseling.

Any woman, regardless of her age, marital status or childbearing experience, may go to a Title X-funded clinic for family planning services. However, the amount each individual pays for the services she receives depends on her income. If she is very poor (her income is at or below 100% of the federal poverty level), the law requires that she receive fully subsidized services. If her income is above 250% of poverty, she must pay the full fee charged by the clinic, and if it falls in between, she must be charged for services on a sliding-fee scale.

The Title X program also supports three functions aimed at assisting clinics to respond to clients' changing needs. To foster consistently high standards in the delivery of family planning services, Title X supports centralized training in each of the 10 federal health regions and is a major source of funding for five of the nation's accredited nurse practitioner training programs. Title X specifically authorizes research to improve the delivery and efficiency of family planning services nationwide. Third, Title X requires that information be collected on the program and its clients and provided periodically to Congress.

Title X and Politics

As the one federal program devoted to the provision of family planning services,

Title X has been the focal point for much of the political wrangling over reproductive health issues.

Eliminating Title X. In 1995, Rep. Bob Livingston (R-LA) proposed eliminating the Title X program and reallocating its funds to the maternal and child health block grant and community and migrant health centers—without requiring that any of the reappropriated funds be spent to provide family planning services. He and his supporters argued that Title X should be turned over to the states to permit maximum flexibility in the provision of health care services, reviving the long-standing debate over whether responsibility for the nation's social programs should rest with the federal government or the states.

Opponents of the Livingston amendment maintained that states wishing to administer the Title X program are already free to do so under the law and that passage of the amendment would jeopardize the existing network of clinics; the 25% of U.S. counties dependent solely on family planning service providers supported by Title X would be at risk of losing their family planning providers. Moreover, because of restrictions in the maternal and child health law, 30% of the funds at most could be spent to provide family planning. In the end, the House chose to maintain Title X as a discrete health program, defeating the Livingston amendment by a vote of 221-207.

Title X and Teenagers. From its inception, Title X has required that services be made available without regard to age or marital status. Consequently, Title X-supported clinics have always provided confidential services to adolescents who request them.

This fundamental underpinning of the program was challenged in 1996, when Rep. Ernest Istook (R-OK) offered an amendment that would have required family planning providers to obtain written parental consent for most minors seeking services at Title X-funded clinics.

The issue of adolescents' ability to consent to their own health care had not been confronted to such an extent since the Reagan administration proposed new Title X regulations in 1982, which were popularly known as the "squeal rule." While citing as its legal basis a congressional mandate from the previous year that Title X-funded clinics "to the extent practicable...encourage family participation" in minors' family planning decisionmaking, the squeal rule would have gone further to *require* clinics to notify parents by registered mail of their children's visit to a family planning clinic. Although more than 40,000 letters of protest were filed with DHHS from medical, health and civic groups, the regulations were finalized in 1983. But two federal appeals court judges eventually barred enforcement, and the regulations were withdrawn before going into effect.

Proponents of the 1996 Istook amendment stated their objections to the use of federal tax dollars to fund contraceptives for their children without their knowledge. In response, the amendment's opponents pointed out that the majority of teenagers do not come to family planning clinics until they have already been sexually active for at least a year, and that creating additional delays could discourage adolescents who are trying to take responsibility for their lives by protecting themselves against unintended pregnancies and STDs.

In the end, a substitute amendment requiring Title X grantees to certify to the DHHS secretary that they encourage family participation in line with their long-standing mandate to do so prevailed by a vote of 232-193.

Title X and Abortion. From the beginning, the Title X statute has prohibited use of the program's funds for "abortion as a method of family planning." Congressionally requested investigations in the 1980s repeatedly found that all Title X-supported clinics were operating in full compliance with the law.

However, counseling regarding the management of an unintended pregnancy and referrals for requested medical and social services not offered by Title X are standard practice and are required by the program's guidelines. Nonetheless, in 1987, President Ronald Reagan ordered DHHS to promulgate new regulations that would have prohibited doctors and other health care professionals working in Title X-funded clinics from providing any abortion-related information or referrals.

The regulations generated more than 75,000 comment letters. Thirty-six state governments and a host of national health, medical and civic groups wrote in opposition to the proposed rules, expressing concern that withholding this information would violate their medical ethics and standards. Moreover, they pointed out, many of the women who depend upon Title X services often have no other source for this information.

While the legality of the so-called "gag rule" was upheld by the U.S. Supreme Court in 1991, Congress later passed legislation to overturn it. President George Bush vetoed the legislation, but a series of last-minute court orders blocked the regulations' enforcement. They were ultimately withdrawn in 1993 at the direction of President Bill Clinton.

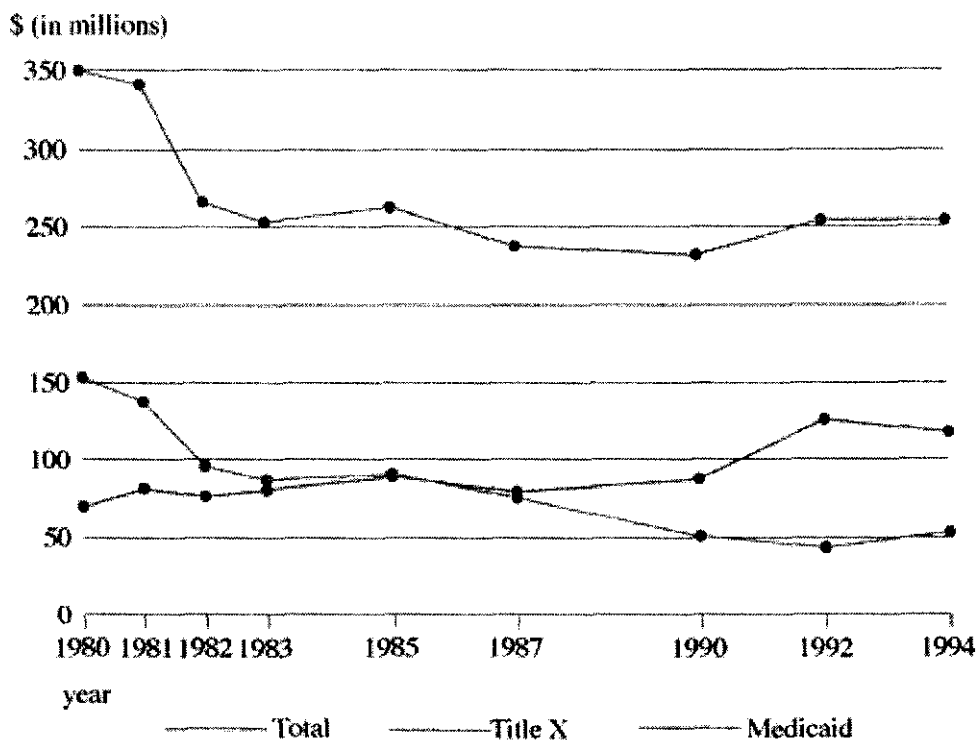
Looking Ahead

Over the last decade or so, the proportion of public funding for family planning services from different sources has shifted greatly. Of the \$715 million spent by all public sources—federal and state—to provide contraceptive services in 1994, \$332 million, or 46%, was spent under Medicaid. In contrast, the Title X program, through which \$151 million was spent for contraceptive services, accounted for only 21%.

In constant dollars—that is, dollars adjusted for inflation—Title X expenditures for contraceptive services decreased by 65% between 1980 and 1994. Despite a 70% increase in Medicaid, *total* public expenditures for contraceptive services dropped by 27% during that period (see Chart B).

Chart B: Funding Trends

Spending for family planning, in constant 1980 dollars, is down.



At the same time, the cost of providing certain family planning services, such as contraceptive supplies and related laboratory expenses, appears to have risen: Between 1991 and 1992, the average price that publicly funded clinics paid for oral contraceptives rose 42%, for example.

Furthermore, many individuals who seek reproductive health care at family planning clinics often have other health care needs. In recent years, for example, the proportion of patients coming to family planning clinics in need of screening or treatment for STDs has increased dramatically. Forty percent of all medical visits to one Title X grantee in 1990 involved testing or treatment for STDs, compared with only 10% of visits in 1980. By 1993, STD and AIDS counseling, testing and treatment constituted, on average, 26% of the contraceptive services budgets among the agencies that offered these services.

Moreover, since clients of Title X-supported clinics frequently have no other source of health care, clinics must address patients' health needs more comprehensively, by offering such corollary health services as screening for diabetes or high cholesterol levels, programming on prenatal care or smoking cessation, and counseling on domestic violence or substance abuse. All of these efforts consume additional resources, in both staff time and money, usually without extra funding from any source.

Some providers cannot absorb these additional costs without cutting back on their patient populations. Others are forced to forgo routine testing and to base treatment on examinations alone. Still others must change the nature of their services, by requiring fees or taking a higher proportion of clients who can afford to pay. For poor women seeking to prevent unintended pregnancy—particularly many of those who may be leaving the welfare rolls in light of the 1996 welfare reform law—some of these changes could present insurmountable

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obstacles.

Despite growing enrollment in managed care plans nationwide, the need for the reproductive health services provided by publicly funded family planning clinics remains crucial for many low-income women, especially those who are uninsured. Even women who have some type of health care coverage continue to seek care at family planning clinics—whether or not those clinics are participating in managed care networks—because their plans do not cover the contraceptives they want or because of concerns about confidentiality.

Despite the continuing need for subsidized family planning services, some critics argue that Title X should be defunded entirely because it has failed to solve our national problems of unintended teenage pregnancy and out-of-wedlock births. Some even go so far as to claim that contraception itself is a failure, and that the provision of publicly funded family planning services has made these problems worse.

Yet incontrovertibly, contraception works: While no contraceptive, and no contraceptive user, is perfect, the fact remains that the 10% of American women at risk of unintended pregnancy who do not practice contraception account for 53% of all unintended pregnancies. Even the strongest supporters of the national family planning program readily admit that it will never, by itself, reduce the nation's unintended pregnancy rate to zero. Nevertheless, they also point out that the availability of affordable, voluntary family planning services remains the only programmatic intervention that—in a cost-effective manner—has a demonstrated ability to reduce unintended pregnancy, avert the need for abortion and improve birth outcomes and the overall reproductive health of women in the United States.

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GYNECOLOGY

A comparison of different laparoscopic sterilization occlusion techniques in 24,439 procedures

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This investigation assessed the safety and efficacy of five laparoscopic tubal occlusion techniques for female sterilization: electrocoagulation, the tubal ring via conventional and open laparoscopy, the prototype spring-loaded clip, and the Rocket clip. The 24,439 cases make up a data set collected by collaborating staffs at 64 institutions in 27 countries. The five techniques were compared with respect to six commonly evaluated parameters. Rates of surgical difficulties ranged from 2.4% to 12.5% (5.1% overall); rates of surgical complications, from 0.7% to 2.7% (1.7% overall); and rates of technical failures, from 0.6% to 1.0% (0.8% overall). Twelve-month life-table pregnancy rates were less than one per 100 woman years. Prospective data on six menstrual parameters revealed that the menstrual cycles of the majority of women were unchanged after sterilization; for those who reported a change, approximately half experienced a change in one direction and half in the other direction. For example, one half reported an increase in the amount of menstrual flow, and one half reported a decrease in the amount of flow. The reported incidence of subsequent pelvic operations was less than 1% at each long-term follow-up. These data indicate that laparoscopic sterilization is safe and effective and that none of the studied techniques has a distinct advantage. (AM. J. OBSTET. GYNECOL. 144:319, 1982.)

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Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study

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Objective: To assess the safety, acceptability, and economy of local anesthesia and intravenous (IV) sedation versus short-term general anesthesia for laparoscopic sterilization.

Methods: We randomly allocated 125 of 150 consecutively sterilized women to either local or general anesthesia. No women were excluded, but 25 chose not to participate. The women were interviewed before surgery, and they returned a standardized questionnaire after discharge from the hospital. All laparoscopic tubal sterilizations were performed by senior gynecologists. Midazolam was used as premedication. In the local-anesthesia group, lidocaine with adrenaline was infiltrated infraumbilically and bupivacaine was applied to each tube. Midazolam and alfentanil were used as IV sedation. In the general-anesthesia group, intubation anesthesia was accomplished with alfentanil and propofol; atracurium was used for muscle relaxation.

Results: In the local-anesthesia group, operation time was shorter, perioperative discomfort was modest, and the costs of equipment were lower than in the general-anesthesia group. There was less postoperative abdominal pain and less need of analgesics, and the patients were more awake in the evening. The rise in heart rate and blood pressure were higher in the local-anesthesia group, and external oxygen was necessary to avoid apnea. Anesthetic surveillance was therefore mandatory.

Conclusions: Local analgesia was highly acceptable to the majority of patients as well as to the gynecologists. The operation time was less, postoperative recovery was quicker, and the women were less bothered by abdominal pain and sore throat. There was a substantial reduction in anesthesia costs. Anesthetic surveillance during surgery was necessary. (*Obstet Gynecol* 1993;81:137-41)

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May 11, 2001
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Fact Sheet

Pregnancy-Related Mortality

- Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native women suffer a significantly higher risk of pregnancy-related mortality than non-Hispanic white women, while black women continue to have the highest risk of all of these racial and ethnic groups.
- There were 3193 pregnancy-related deaths between 1991 and 1997 in the United States. This results in an overall pregnancy-related mortality ratio (PRMR) of 11.5 per 100,000 live births.
- Hispanic women had a PRMR of 10.3 for the study period, while Asian/Pacific Islanders and American Indian/Alaska Natives had higher PRMRs, 11.3 and 12.2 respectively. In comparison, non-Hispanic whites had a PRMR of 7.3 and blacks had a PRMR of 29.6.
- The risk of a pregnancy-related death was lowest for women under the age of 30, rising after the age of 35, for all of the racial and ethnic groups where there was a large enough number to analyze.
- Place of birth, within the United States or elsewhere, was also related to the PRMR for some racial and ethnic groups. Hispanic women born outside of the United States had nearly a 50% higher PRMR than Hispanic women born within the United States.
- Women of Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native origin represented 16% of the reproductive-age population in 1997, but accounted for nearly a quarter of all of the live births in the United States. The Census Bureau projects by 2025, women of these racial and ethnic groups will make up a quarter of the women in the United States.
- A pregnancy-related death is defined as a death that occurred to women during their pregnancy or within one year after the end of the pregnancy, resulting from pregnancy complications or effects.

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Safe Motherhood

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Safe Motherhood: Promoting Health for Women Before, During, and After Pregnancy 2002

At A Glance 2002

"We as a nation must do all we can to ensure that all mothers are safe and healthy before, during, and after pregnancy. Every year, nearly 1,000 of our sisters and daughters die and hundreds of thousands of others experience medical complications from pregnancy. Death and serious illnesses due to pregnancy and childbirth shouldn't be part of the picture in the United States."

Wanda K. Jones, DrPH
Deputy Assistant Secretary for Health (Women's Health)
Director, Office on Women's Health, U.S. Public Health Service

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Safeguarding the Health of Mothers

Approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Safe motherhood begins before conception with proper nutrition and a healthy lifestyle. It continues with appropriate prenatal care, the prevention of complications when possible, and the early and effective treatment of any complications that do occur. The ideal result is a labor at term without unnecessary interventions, the delivery of a healthy infant, and a healthy postpartum period in a positive environment that supports the physical and emotional needs of the woman, infant, and family.

Deaths From Pregnancy Complications: No Decline in 20 Years

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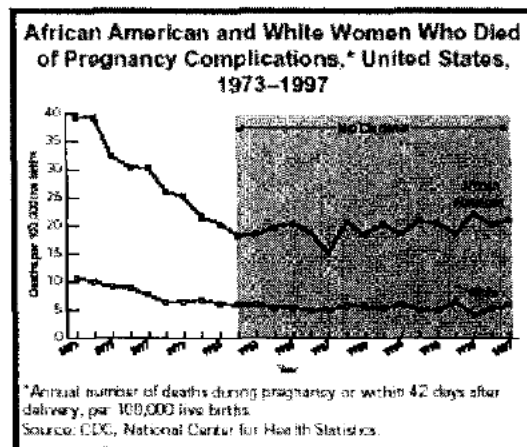
Each day in the United States, two to three women die of pregnancy complications. From 1900 to 1982, deaths from pregnancy complications in the United States declined dramatically. Since 1982, however, deaths stopped declining, and there has been no further improvement. Studies indicate that as many as half of all deaths from pregnancy complications could be prevented through broader access to health care, better quality of care, and changes in health and lifestyle habits.

The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy (heart muscle disease).

Large Racial, Ethnic, and Age Disparities

A woman's race, ethnicity, country of birth, and age are associated with her risk of dying from pregnancy complications. For example,

- African American women are 4 times as likely to die of pregnancy complications compared with white women, and American Indian and Alaska Native women are nearly twice as likely to die.
- Asian and Pacific Islander women who immigrated to the United States are twice as likely to die of pregnancy complications as those born in the United States. Hispanic women who immigrated are 1.5 times as likely to die as those born in the United States.
- Women 35–39 years old are nearly 3 times as likely to die of pregnancy complications as women 20–24 years old. The risk of dying is even greater for women over 40.



Deaths Only Part of the Picture

More than one in three pregnant women in this country develop a pregnancy complication. The most common complications include

- Miscarriage
- Ectopic pregnancy
- Hemorrhage
- Infection
- Diabetes
- High blood pressure
- Excessive vomiting

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- Premature labor
- Need for a caesarean delivery
- Depression

Childbirth remains the most common reason for hospitalization in the United States, and pregnancies with complications result in more costly hospitalizations. In the United States, hospitalizations for pregnancy complications before delivery account for more than 2 million hospital days of care each year and cost more than \$1 billion annually. These figures would be even higher if we took into account complications during or after delivery.

Economic costs are not the only concern. Pregnancy complications and deaths also cause pain and suffering. We need to learn more about how pregnancy complications affect women and their infants and families.

CDC's National Leadership and State Partnerships

The Safe Motherhood Initiative

CDC and its many partners are making major strides in safeguarding the health of mothers. Supporters of healthy motherhood include not only health departments and other federal agencies but also universities, private practices, advocacy groups, professional organizations, and businesses. In 2001, CDC and its partners

- Held the first U.S. Summit on Safe Motherhood, which brought together a broad coalition of agencies, organizations, and professionals dedicated to improving maternal health. They discussed the social, economic, and medical aspects of maternal health and called for research, policies, and coordinated action to make maternal health a national priority.
- Published *Strategies to Reduce Pregnancy-Related Deaths: From Identification to Action*. This guide helps states identify maternal deaths, expand the types of data collected about deaths, and apply the findings to protect women's health.
- Published a journal issue devoted to studies of what is unique about the experience of being an African American woman that puts her at higher risk for having a premature baby. Racism, limited health care options, and poor-quality housing are some of the problems explored.
- Expanded the Pregnancy Risk Assessment Monitoring System so that surveys of new mothers are conducted in 32 states and New York City and now cover 62% of all U.S. births.

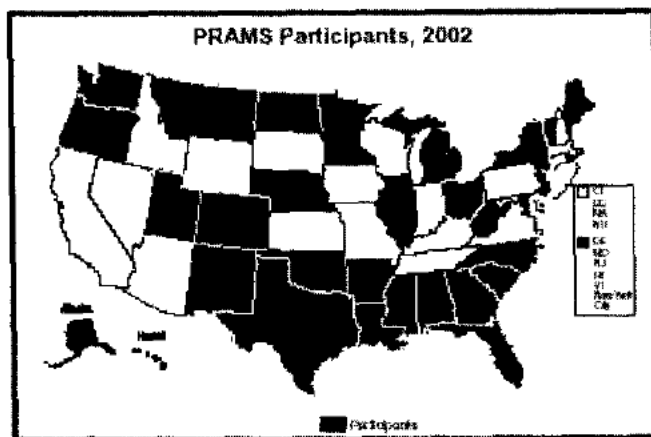
CDC works with states to translate science into quality programs. As partners, CDC and states can reduce pregnancy complications and save lives—by monitoring maternal health, conducting research, and educating people about safe motherhood.

Pregnancy Mortality Surveillance System (PMSS). Through the PMSS, CDC works with state health departments and other organizations to identify and gather information on pregnancy-related deaths. CDC uses PMSS data to examine

- Trends in pregnancy-related deaths.
- Risk factors for pregnancy-related death.
- Disparities related to race, ethnicity, and age.
- Specific conditions leading to death.

Maternal and Child Health Epidemiology Program (MCHEP). This program helps state and local health departments collect and analyze data needed to improve the health of mothers and children. CDC and the Health Resources and Services Administration (HRSA) support the MCHEP. Through the MCHEP, epidemiologists specializing in maternal and child health serve 10 states and two Indian health agencies. MCHEP also provides technical assistance and training to public health staff and sponsors conferences and Internet groups where peers can share their knowledge about maternal and child health.

Pregnancy Risk Assessment Monitoring System (PRAMS). CDC and state health departments use PRAMS to collect state-specific, population-based data on women's behaviors and experiences before, during, and immediately after pregnancy. These data identify groups of women at high risk for health problems, monitor changes in health status, and measure progress in improving the health of mothers and infants. PRAMS surveys are now conducted in 32 states and New York City.



Learning More, Making a Difference

Conducting Innovative Research

To learn more about how to improve women's health before, during, and after pregnancy, CDC supports innovative research, including the following projects:

- **Racial and ethnic differences in pregnancy complications and deaths.** One of the greatest racial gaps in public health is the fact that African American women are four times as likely as white

women to die of pregnancy complications. CDC is examining national data to find out why the risks for complications and deaths are so much greater among these women. CDC also is collaborating with researchers in North Carolina to explore whether African American women have more severe pregnancy complications than white women and whether they receive different treatment when they seek medical care for pregnancy complications.

- **Intimate partner violence among pregnant women.** Each year, up to 300,000 pregnant women in the United States are victims of intimate partner violence. Violence is more common among pregnant women than many conditions for which they are routinely screened. CDC and the American College of Obstetricians and Gynecologists developed training materials clinicians can use to screen women for violence during prenatal care visits. Moreover, CDC is funding an evaluation of a model intervention in which screening for violence is a routine part of obstetric and gynecological care. This evaluation also will help determine whether abused women who are identified through screening get the help they need.
- **Effects of high-tech infertility treatments.** In vitro fertilization and other high-tech infertility treatments are an increasingly common choice for the estimated millions of couples who face infertility each year. In 1999, more than 86,000 such procedures were performed in the United States, and over 30,000 babies were born as a result. CDC is now working with Massachusetts to study how these procedures affect the health of mothers and their infants.

Gathering Strong, Useful Data

Here are some of the ways that CDC and its partners are addressing the need for more complete and accurate information about pregnancy complications and deaths:

- Working with researchers in Oregon, Washington, and Illinois to find the best ways to identify and monitor pregnancy complications and risk factors.
- Collaborating with researchers in six cities to better understand how stress and infections affect the health of pregnant women and their babies.
- Expanding PRAMS and MCHP to more states, strengthening the states' ability to identify and address maternal and child health problems.
- Analyzing national and state data to learn more about pregnancy complications and to identify factors involved when a woman dies or almost dies of pregnancy complications.

Educating and Training Others

CDC works with many partners to share knowledge about safe motherhood. For example, CDC is


- Identifying strategies that health care providers can use to reduce pregnancy complications.
- Reporting trends in maternal and child health for states to use in program planning.
- Training public health professionals to better understand maternal


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and child health problems and potential solutions.

- Working with women in Los Angeles communities to develop educational materials that will help pregnant women recognize the warning signs of preterm labor.
- Producing a *Maternal and Child Health Journal* issue highlighting the latest research on the health of women before, during, and after pregnancy.

CDC also helped to prepare *Healthy People 2010* goals that aim to dramatically improve the health and wellbeing of mothers in America over the next decade. To help the nation meet these goals, CDC will work with other federal agencies, states, nonprofit organizations, and community groups. As partners, we can make safe motherhood a reality.

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Complications of Interval Laparoscopic Tubal Sterilization

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In 1978, the Centers for Disease Control initiated a multi-center prospective study to assess the safety of the various female sterilizing operations and the ways in which they could be made safer. During the first 31 months, 3500 women who underwent interval laparoscopic tubal sterilization by electrocoagulation or Silastic banding without other concurrent operations were enrolled in the study. When a standard definition of complications was used, the overall rate of an intraoperative or postoperative complication was 1.7 per 100 women. Several patient factors increased the risk of complications twofold or more: diabetes mellitus, previous abdominal or pelvic surgery, lung disease, a history of pelvic inflammatory disease, and obesity. There was a fivefold difference in complication rates between procedures performed under general anesthesia and those done under local anesthesia. (*Obstet Gynecol* 61:153, 1983)

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identified in this study were those performed under local anesthesia.

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Contraception 62 (2000) 169-175
Original research article

Two randomized controlled trials comparing the Hulka and Filshie Clips for tubal sterilization

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Abstract

To compare the effectiveness and safety of the Filshie Clip System™ and Hulka Clip System when applied via minilaparotomy and laparoscopy, we conducted 2 multicenter randomized controlled trials of 2126 women (878 in the minilaparotomy study and 1248 in the laparoscopy study) who received either the Filshie or Hulka Clip. A physician other than the operator evaluated patients postoperatively and again at 1, 6, and 12 months after surgery. We compared the cumulative incidence of pregnancy and the frequency of safety related events for the device groups. Twenty-four month follow-up was planned for a subset of 599 women in the laparoscopy study. One woman who received the Filshie Clip and 6 women who received the Hulka Clip became pregnant within one year. The 12-month life-table pregnancy probability was 1.1 per 1000 women in the Filshie Clip group and 6.9 per 1000 women in the Hulka Clip group. The difference in the risk of pregnancy through 12 months between device groups neared statistical significance ($p = 0.06$). Among the extended follow-up subset, the 12- and 24-month cumulative pregnancy probabilities were 3.9 and 9.7 per 1000 women for the Filshie Clip group and 11.7 and 28.1 per 1000 women for the Hulka Clip group ($p = 0.16$ for comparison through 24 months). Both the Filshie and Hulka Clips are effective and safe for use in tubal occlusion. © 2000 Elsevier Science Inc. All rights reserved.

Keywords: Tubal occlusion devices; Female sterilization; Filshie Clip; Hulka Clip

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Hospitalization for pregnancy complications, United States, 1986 and 1987

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OBJECTIVE: The purpose of our analysis was to provide a national overview of the magnitude of the public health burden associated with inpatient care for pregnancy complications.

STUDY DESIGN: We analyzed data from the National Hospital Discharge Survey for 1986 and 1987. We calculated ratios of hospitalizations for pregnancy complications for every 100 hospitalizations involving a birth. Standard errors for these ratios were calculated with RATIOEST, and relative ratios with 95% confidence intervals were calculated for subgroups of interest.

RESULTS: We found that for every 100 hospitalizations involving a birth, there were 22.2 nondelivery hospitalizations for pregnancy complications (14.6 antenatal complications, 7.6 pregnancy loss complications). These ratios were higher for black than for white women (relative ratio 1.4, 95% confidence interval 1.2 to 1.6). The effects of marital status, age, and insurance coverage differed between black and white women, and mean length of stay was longer for black than for white women.

CONCLUSION: Hospitalization for pregnancy complications is far more common than is widely appreciated and is more frequent among black than white women. (*AM J OBSTET GYNECOL* 1992;168:1339-44.)

Key words: Maternal morbidity, pregnancy complications, hospitalization, race

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The prevalence and impact of pain after day-care tubal ligation surgery

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Summary Empirical data from controlled studies using standardized, reliable measures on the amount and quality of pain after laparoscopic tubal ligation and the consequences of this pain on the activities of daily living are extremely scarce. In a study of 54 women admitted to a day-care unit for this procedure, validated measures were utilized to assess the incidence, intensity and duration of pain after tubal ligation (McGill Pain Questionnaire) and the impact of pain on the activities of daily living (Modified Functional Assessment Inventory). Psychological measures (Brief Symptom Inventory, Krunk Health Opinion Survey, and the State-Trait Anxiety Inventory) were employed to test their use as possible predictors for pain, analgesic usage and the time taken to resume a normal activity level after tubal ligation surgery. The results showed that pain is a significant problem after tubal ligation although pain rating scores over the 7-day study period were lower than those reported after major abdominal surgery. Eighty-five percent of our sample reported that pain and/or fatigue impacted on their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of surgery.

The psychological measures did not prove to be strong predictors of postoperative pain, time of return to normal activity level or analgesic usage. The most powerful predictor of return to normal activity was the total amount of pain experienced, as measured by the McGill Pain Questionnaire, during the 7 day post-operative period.

Key words: Pain; Tubal ligation; Sterilization; Day-care surgery

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Economic and Clinical Outcomes of Microlaparoscopic and Standard Laparoscopic Sterilization

A Comparison

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Francisco A. R. Garcia, M.D., M.P.H., Ina Steinmetz, M.D., Bel Barker, M.D., and George R. Huggins, M.D.

OBJECTIVE: To compare microlaparoscopic surgical sterilization and standard laparoscopic sterilization with respect to cost effectiveness and patient preferences.

STUDY DESIGN: A retrospective study of all laparoscopic surgical sterilizations performed under general anesthesia at Johns Hopkins Bayview Medical Center—

16 microlaparoscopies and 34 standard laparoscopies. Cases selected for review were limited to patients undergoing surgical contraception and not requiring additional, concurrent procedures. Laparoscopic surgical sterilization was performed using a double-puncture technique with silicone band application. In each case either a standard, 10-mm laparoscope or a 2-mm microlaparoscope was used, and the procedure was performed under general anesthesia. Postoperative pain management was

achieved by nonsteroidal antiinflammatory drugs and/or narcotic analgesia. All cases were performed by residents under faculty supervision.

Medical records and hospital billing records were reviewed, and a standardized telephone interview was conducted to assess postoperative quality of life and patient satisfaction.

A statistically greater number of subjects in the microlaparoscopic group reported overall satisfaction....

RESULTS: Both techniques were comparable in cost effectiveness. There was no significant difference in operating room time, average operating room costs, average ancillary department costs, instrument and supply costs, or length of stay. Postoperative discomfort was significantly less with microlaparoscopy ($P = .05$), and patient satisfaction was higher in the microlaparoscopy group.

CONCLUSION: Microlaparoscopy and the standard laparoscopic approach for surgical sterilization are asso-

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GLOBAL HEALTH OPTIONS

BIRTH CONTROL AND UNINTENDED PREGNANCIES

- This section explores the relationship between **Birth Control** and **Unintended Pregnancies** in the USA

INTRODUCTION - DATA

- Approximately 5.38 million pregnancies occur in the USA each year.
- Almost half (49% or ~2.65 million) of these are unintended pregnancies.
- Of the unintended pregnancies 46% (~1.2million) result in births and 54% (~1.4million) end in abortion.
- Teenagers (ages 15 -18) have the highest rate of unintended pregnancies.
- Surprisingly, the second highest rate is found in women aged 40 - 44 years.
- Only 40% of unintended pregnancies occur in women who do not use any form of birth control.
- The majority, 60%, occur in women using some form of birth control. This translates into approximately 1.4 million unintended pregnancies occurring in women using birth control at the time that they become pregnant.
- It is estimated that about 1 million unintended pregnancies happen because of improper use of Oral Contraceptives (Birth Control Pills).

DISCUSSION

- The rate of unintended pregnancies in the USA is quite high in comparison to the other developed nations of the world.
- The overall rate of unintended pregnancies has declined little over the past several decades.
- Given the above facts, it may be argued that unintended pregnancy represents an important public health concern in the USA.
- There are many risks and consequences associated with an unintended pregnancy; while abortion and negative socioeconomic issues are usually the predominant focus, the mortality and morbidity associated with a pregnancy in this context are very important and frequently overlooked.
- For example, consider the following. Childbirth is the most common reason for hospitalization in the USA and hospitalizations for pregnancy complications occurring before delivery account for more than 2 million hospital days per year, at a cost of greater than \$1 billion annually.
- For the overwhelming majority of women, effective contraception is much safer than childbirth.
- In 1995, 17.6 million women visited their health care providers to receive services for a Birth Control method. However, studies have found that women reported using some form of Birth Control during the month of conception for more than half (53%) of all unintended pregnancies.
- In this population of women, unintended pregnancy results from inconsistent or improper use of Birth Control, often Oral Contraceptives (Birth Control Pills).
- Women point to several reasons for inconsistent or improper use of Oral Contraceptives (Birth Control Pills). The major ones are : difficulties associated with remembering to take a pill every day, tolerability issues, especially breakthrough bleeding, and fears about the potential risks of Oral Contraceptive (Birth Control Pill) use.

CONCLUSION

- There is a very high number of unintended pregnancies occurring in the USA each year.
- An unintended pregnancy can have long-lasting and potentially dangerous medical consequences.
- By contrast, a planned pregnancy can facilitate an optimal outcome for both mother and offspring. The benefits of planning a pregnancy extend not only to the psychosocial and economical aspects but, most importantly, to the health aspects.
- For example, planning a pregnancy allows for the treatment of any preexisting medical conditions and the prevention or treatment of any potentially harmful infections while at the same time allowing for proper immunization management of the mother-to-be.
- Millions of women become pregnant despite using a method of Birth Control at the time of conception.
- While there are many factors that can contribute to the aforementioned failure of contraceptive methods, a large number of women report incomplete or improper use of Birth Control due either to intolerance of or displeasure with the side-effects of the method, or to misperceptions about the potential risks of using a particular method of Birth Control.
- In conclusion, the prevention of unintended pregnancies represents an important health concern and a challenge for both the public and the medical profession, in particular.
- Steps that might be considered in reducing unintended pregnancies are :
 - 1) Better informing the public about this problem and its implications.
 - 2) Better educating patients in the correct use of the available methods of Birth Control and dispelling the misconceptions about them.
 - 3) And most importantly, making available to the public as wide an array of Birth Control options as possible and continuing research efforts.

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MISSION

Global Health Options wants to expose a worldwide audience to health information and products. The goal is to empower people to live a healthier life, gain a better understanding of their body, and have an optimal experience in times of illness.

HISTORY

Global Health Options arose from a need to inform the public about the great divide that exists in the arena of Birth Control, particularly between the Americans and their European counterparts. According to Dr. Felicia Stewart, a Birth Control expert that served in the Clinton administration: **'Women and men in the United States don't know that they're being shortchanged.'**

The options for Birth Control methods are far greater in Europe vs. the USA. What is perhaps even more troubling then that is the fact that a lot of the Birth Control options available in Europe have been developed in the USA and, sometimes, even tested on American women. Thus, Global Health Options presents information and, occasionally, products to the public in an effort to educate and improve the health of all people, regardless of geographical boundaries.

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Abortion Patients in 1994-1995: Characteristics and Contraceptive Use

By Stanley K. Henshaw and Kathryn Kost

Results of a 1994-1995 national survey of 9,985 abortion patients reveal that women who live with a partner outside marriage or have no religious identification are 3.5-4.0 times as likely as women in the general population to have an abortion. Nonwhites, women aged 18-24, Hispanics, separated and never-married women, and those who have an annual income of less than \$15,000 or who are enrolled in Medicaid are 1.6-2.2 times as likely to do so; residents of metropolitan counties have a slightly elevated likelihood of abortion. When age is controlled, women who have had a live birth are more likely to have an abortion than are those who have never had children. Catholics are as likely as women in the general population to have an abortion, while Protestants are only 69% as likely and Evangelical or born-again Christians are only 39% as likely. Since 1987, the proportion of abortions obtained by Hispanic women and the abortion rate among Hispanics relative to that for other ethnic groups have increased. The proportion of abortion patients who had been using a contraceptive during the month they became pregnant rose from 51% in 1987 to 58%. Nonuse is most common among women with low education and income, blacks, Hispanics, unemployed women and those who want more children. The proportion of abortion patients whose pregnancy is attributable to condom failure has increased from 15% to 32%, while the proportions reporting the failure of other barrier methods and spermicides have decreased. (Family Planning Perspectives, 28:140-147 & 158, 1996)

Annual national data describing women having abortions in the United States cover only basic demographic characteristics--age, race, ethnicity, marital status, and prior births and abortions--as well as the procedure used for the abortion and the length of the pregnancy. This information is collected by most states, and it is compiled and published at the national and state levels by the Centers for Disease Control and Prevention (CDC). However, some states have no abortion reporting system, and the CDC reports understate the number of abortions performed. The Alan Guttmacher Institute (AGI) conducts periodic surveys of all abortion providers throughout the country and uses the results together with the CDC data to estimate the number of abortions nationwide and the abortion rate according to a variety of characteristics.¹

This article reports information from a 1994-1995 AGI survey detailing a broad range of characteristics of abortion patients--socioeconomic status, religious affiliation, residence, childbearing intention and contraceptive use prior to the pregnancy. The survey, part of a larger project to update contraceptive failure rates, obtained usable questionnaires from 9,985 respondents in a stratified national sample of 100 clinics, hospitals and physicians' offices in all regions of the country. This information updates the findings from a similar 1987 survey of 9,480 abortion patients in a stratified national sample of 103 facilities.²

Methodology

Data Collection

Data were collected by means of a self-administered questionnaire, available in both English and Spanish, which the staff of abortion facilities distributed to patients. The facilities decided when to present the questionnaire to patients; most gave it to women to complete along with other paperwork while they waited for the procedure. Attached to the questionnaire was an introduction explaining that the survey was voluntary, anonymous and for research only.

The questionnaire was a single sheet of paper with questions on both sides covering women's characteristics and prior contraceptive use. Because data from the 1995 National Survey of Family Growth (NSFG) were to be used in conjunction with findings from this survey to calculate contraceptive failure rates, the questions had been slightly revised since 1987, to replicate to the extent possible those used in the 1995 NSFG.

The facilities selected for the study were drawn from a list of all hospitals, clinics and physicians' offices where abortions are performed. The list, which had been updated in 1993 for AGI's periodic survey of abortion providers, was stratified by provider type (hospital or nonhospital facility) and by the number of abortions performed in 1992, rounded to the nearest 10 (30-390; 400-1,990; 2,000-4,990; or 5,000 or more). Facilities that reported fewer than 30 abortions were impractical to survey, but their exclusion would cause little bias, since they accounted for only 0.4% of all reported abortions in 1992.³

Within each stratum, facilities were listed by state, and states were arranged geographically within census region; for our analysis, we selected facilities at equal intervals on the list (such as every fifth or every seventh one), depending on the stratum. Each facility was asked to administer the questionnaire to every woman who obtained an abortion during a specified time period ranging from two to 12 weeks, depending on the facility's caseload. If a facility declined to participate or did not obtain usable questionnaires from at least half of the target women throughout the specified time, it was replaced by the next facility on the list, which in most cases was in the same or a neighboring state and in the same region.

We initially sampled 113 abortion providers--19 hospitals and 94 nonhospital facilities. Of these, 11 and 46, respectively, had to be replaced--31 facilities were unable or unwilling to participate, 11 had closed, 11 were unable to administer the survey for the required number of weeks or had a response rate of less than 50%, and four had caseloads that had fallen below 30 per year. (In some cases, the replacement facilities also had to be replaced.) Nine of the hospitals and 18 of the other facilities that had to be replaced performed 30-390 abortions a year. Since facilities of this size provide only 9% of all abortions, selection bias among them would have had only a small effect on the sample. We ultimately obtained usable data from 13 hospitals and 87 nonhospital facilities; the 13 facilities that could not be replaced were in the smallest caseload category.

Participating facilities were asked to report the number of abortions they performed during the specified time frame; the total came to 11,288. Usable questionnaires were obtained from 9,985 of the women, for a response rate of 88%. At our request, the providers supplied information about the age, race, ethnicity and Medicaid coverage of 562 nonrespondents; no information was available for the remaining 741 nonrespondents. Most nonresponse resulted

from women's refusal to participate, facilities' failure to distribute questionnaires or lack of time for the patient to complete the questionnaire. Of the usable responses, 87% were obtained during the second half of 1994 and 13% during the first half of 1995.

To correct for any bias produced by deviation from the original sampling plan and nonresponse, a three-stage weighting process was followed. First, individual weights were developed to adjust for the demographic characteristics of the 562 nonrespondents for whom the facilities provided data. Second, facility-level weights were used to adjust for the other 741 nonrespondents. Third, stratum weights were constructed to correct for departures from the number of facilities to be sampled in each grouping by caseload and provider type. With the final weight adjusted to a mean of 1.0, the standard deviation was 0.22 and the range was 0.54-3.27.

The rate of nonresponse on individual items was generally 2-4%, but ranged from less than 2% on Medicaid coverage to 20% on household income. Instead of assuming that the nonrespondents were similar to all those who had answered a question, we imputed missing information on the basis of the responses of other women with similar characteristics, using a "hot-deck" procedure.*

For a sample of 9,985, the 5% confidence interval is $\pm 1\%$ for a proportion of 50%, and less for proportions other than 50%. Because the sample was clustered and weighted, we have used the 3% significance level, for which the confidence interval is $\pm 1.1\%$ or less. All of the differences noted in this article are significant at the 3% level. Since nonrandom error is always a possibility in survey research, however, one should be cautious in drawing conclusions from small differences.

Representativeness of the Survey

As a check on the representativeness of the survey, we compared the results with the adjusted CDC compilations of state reports for 1991,⁴ the latest year for which detailed statistics have been published. **Of the characteristics on which comparisons were possible (age, race, ethnicity, marital status, parity and number of prior abortions), the results were within two percentage points of each other for all subgroups except "other" race (not white or black) and Hispanic ethnicity.

In our survey, 8% of abortion patients reported their race to be Asian, Pacific Islander, American Indian or Alaskan native; in the adjusted CDC statistics, by comparison, the proportion in these racial groups is 4%. There are three possible reasons for the discrepancy: First, the 1991 CDC statistics include no data on abortion patients' characteristics for California, which has a large Asian population. Second, in the AGI survey, 12% of those who reported their ethnicity as Hispanic, a relatively large proportion, reported their race as American Indian or Asian; clinic staff who complete state abortion reporting forms probably tend to record Hispanics as white or black. Excluding Hispanic women, 5% of respondents in the AGI survey were of races other than white or black. Third, the proportion of Asians in the U.S. population grew between 1991 and 1994-1995.

An even larger percentage-point difference emerged in the proportion of women reported to be Hispanic: 20% in the survey and 13% in the adjusted CDC statistics. One possible explanation for this difference is that the survey may have sampled facilities that happened to have a large proportion of Hispanic patients. Since Hispanic patients tend to be concentrated

in certain clinics and in certain states, the survey design produces a higher standard error for this characteristic than for variables that are more uniformly distributed among facilities.

Two other factors, however, could have caused the state statistics compiled by the CDC to underestimate the proportion of Hispanics among women having abortions. First, as noted, characteristics are not known for abortion patients in California, which has both a high abortion rate and a high proportion of Hispanics. Second, CDC reports have indicated that sharp increases have occurred in the proportion of abortions obtained by Hispanic women: 10% in 1990, 14% in 1991 and 15% in 1992.⁵ While this rate of increase is unlikely to continue, the Hispanic proportion may well have been higher in 1994-1995 than it was in 1991.

Overall, the comparison with adjusted CDC data offers reassurance that the survey accurately represents the universe of women having abortions. Even if the survey represented the universe perfectly, some differences between the two data sources would be likely because the 1991 CDC data are based on only 45-55% of all abortions, depending on the characteristic, and on only 33% of abortions among Hispanic women. In addition, changes may have occurred between 1991 and 1994-1995.

Abortion Indices

We were unable to calculate the abortion rate (the number of abortions per 1,000 women) for each subgroup because the total number of abortions performed in 1994 or 1995 is unknown. Instead, we have created an abortion index that allows subgroups to be compared in the same way they could be if their rates were known.

The index is equivalent to the ratio of the abortion rate for each subgroup to the overall abortion rate. It is calculated by dividing the proportion of abortion patients in a subgroup by the proportion of U.S. women 15-44 in that subgroup. *** An index value of 1.0 would indicate that a subgroup's abortion rate was the same as the rate for all women 15-44; values under 1.0 indicate rates below the rate for all women, while values exceeding 1.0 represent above-average rates. The index may be thought of as the "relative abortion rate," since it is the abortion rate of a subgroup relative to that of all women.

Since age is strongly associated with the abortion rate, differences between subgroups may result partly from differences in the ages of women in the subgroups. Therefore, to estimate what the index would be if the age distribution of each subgroup were the same as the age distribution of all women 15-44, we also calculated age-standardized indices for 1994-1995 and for 1987. The age-standardized index for 1987 was derived from the 1987 AGI survey.⁶

Women's Characteristics

Table 1 shows the percentage distribution of women who had abortions and of all women aged 15-44, according to the characteristics about which the survey solicited information. As the table indicates, women aged 20-24 obtain 33% of abortions, and teenagers obtain 22%. Women aged 15-17, with an index of 1.0, are as likely as all women aged 15-44 to have abortions, and those aged 18-19 and 20-24 are about twice as likely to do so (indices of 2.0 and 2.2, respectively). Abortion rates decline sharply in the older age-groups; the likelihood of abortion among women aged 30 and older is no more than 77% of that among all women.

< TD>

< TD>1.23
 < TD>66.2
 < TD>34.4
 < TD>
 < TD>
 < TD>79.6

Table 1. Percentage distribution of U.S. abortion patients, and of all women aged 15-44 and age-standardized index, 1994-1995 and 1987; all by selected characteristics

Characteristic	% distribution	Abortion			Age-standardized			Characteristic	% dist
		index,		index		1987	Ab-		
		Abortion	Women	1994-1995	1994-1995				
		15-44Y							
Age-group							Religion§§ (cont.)		
<15	1.2	u	na	na	na	na	White non-Hispanic		
15-17	8.8	8.8	1.01	na	1.15y		Protestant	1	
18-19	11.5	5.7	2.01	na	2.23y		Catholic	1	
20-24	32.8	15.2	2.16	na	1.95y		All others	6	
25-29	21.4	16.1	1.33	na	1.18y				
30-34	14.4	18.8	0.77	na	0.64y		Born-again/Evangelical		
35-39	7.5	18.6	0.40	na	0.35y		Yes	1	
>=40	2.3	16.8	0.14	na	0.12y		No	8	
Race							Education		
White	61.3	81.2	0.76	0.76	0.83		¾8th grade	4	
Black	31.1	14.0	2.23	2.12	1.99		9th-11th grade	1	
Other	7.6	4.9	1.56	1.55	1.07§		H.S. graduate or GED	3	
							Some college or associate's degree	3	
Ethnicity							College graduate	1	
Hispanic	20.2	10.6	1.90	1.75	1.44				
Non-Hispanic	79.8	89.4	0.89	0.90	0.96				
							Enrolled in school		
Marital							Yes	3	

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status							
Married	18.4	49.9	0.37	0.57	0.52	No	6
Separated	7.2	3.3	2.17	2.83	2.62		
Divorced	9.4	8.6	1.09	1.47	2.05	Currently employed	
Widowed	0.5	0.7	0.78	1.97 ^{ŸŸ}	2.01 ^{ŸŸ}	Yes	
Never-married	64.4	37.5	1.72	1.34	1.35	No	3
Cohabiting						Family income	
Yes	20.2	5.8	3.47	3.06	4.65	<\$15,000	2
No/married	79.8	94.2	0.85	0.86	0.86	\$15,000-\$29,999	1
						\$30,000-\$59,999	3
No. of live births						>=\$60,000	1
0	45.4	41.2	1.10	0.78 ^{ŸŸ}	0.92 ^{ŸŸ}		
1	24.7	18.2	1.36	1.30 ^{ŸŸ}	1.21 ^{ŸŸ}	Has Medicaid coverage	
2	17.8	23.8	0.75	1.25 ^{ŸŸ}	1.03 ^{ŸŸ}	Yes	2
3	7.7	11.1	0.69	1.17 ^{ŸŸ}	1.14 ^{ŸŸ}	No	7
>=4	4.4	5.8	0.76	1.48 ^{ŸŸ}	1.73 ^{ŸŸ}		
						Intends more children	
Religion§§						Yes	6
Protestant	37.4	53.9	0.69	0.73	0.74	No	3
Catholic	31.3	30.9	1.01	0.97	0.95		
Jewish	1.3	1.2	1.08	1.03	0.69	Region of residence	
Other	6.3	8.1	0.78	0.77	2.04	Metropolitan	8
None	23.7	5.9	4.02	3.87	3.68	Nonmetropolitan	1
Total	100.0	100.0	1.00	1.00	1.00	Total	1

ŸData for 1994 except Medicaid status (1993), religion (1993-1995) and childbearing intent
 ŸNot age-standardized. §Not exactly comparable to 1994 because all Hispanics were classified
 44. ŸŸStandardized on women 20-44. §§Based on women 18-44. ŸŸIncome breaks for 1987
 Notes: In this and subsequent tables, na=not applicable; u=unavailable. Sources: POPULA
 F.W. Hollmann and P. Montgomery, "U.S. Population Estimates, by Age, Sex, Race, and Hi
 Projections Branch, U.S. Bureau of the Census, Washington, D.C., 1995. **Marital and coha**
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tabulations of data from five Gallup polls, Roper Center for Public Opinion Research, Storrs
employment status and income--U.S. Bureau of the Census, Current Population Survey, ur
tabulation of the March 1994 Current Population Survey. **Childbearing intentions**--special
Growth. **Metropolitan status**--U.S. Bureau of the Census, *1990 Census of Population, Was*
Population Division, U.S. Bureau of the Census, "Resident Population and Change for Metr
July 1, 1994," PPL -27, Washington, D.C., 1995. **1987 DATA:** See reference 2.

Teenagers' relative abortion rate has declined since 1987, when the index was 1.2 for 15-17-
year-olds and 2.2 for 18-19-year olds. The relative abortion rate increased among women in
their 20s, and the highest rate now occurs among women aged 20 -24, rather than among 18-
19-year-olds.

Although white women obtain 61% of abortions, their abortion rate, reflected by an index of
0.8, is well below that of women of other races. The index for black women is 2.2, or nearly
triple that of white women, and the differential has increased since 1987. The index for
women of races other than black or white is 1.6, but this may be inflated by the inclusion of
some Hispanic women in this group (as explained in the methodology section). In the 1987
survey, which classified all Hispanic women as white or black, the age-standardized abortion
rate for women of "other" races was only slightly above that of all women (1.1); the 1994-
1995 index would be about the same as the 1987 rate if Hispanics were excluded from this
group.

Hispanic women have a much higher abortion rate than non-Hispanics, but their rate is not as
high as that of black women. The index for Hispanics is reduced somewhat when
standardized for age (from 1.9 to 1.8), but is still roughly twice that of non-Hispanic women
(0.9). The age-standardized index for Hispanics has increased substantially from its 1987
level of 1.4.

As they have in the past, never-married women obtain the bulk of abortions (64%); married
women account for only 18% of procedures. The age-standardized abortion rate for married
women is slightly more than half the rate for all women. The rate is highest among separated
women--almost three times the overall rate. Since 1987, the relative rate has decreased
among divorced women.

Women living with a partner to whom they are not married account for 20% of the abortion
sample, but only about 6% of women in the population; their probability of having an
abortion is 4.1 times that of women who are not cohabitating, or 3.6 times after adjustment
for age. The differential appears to have decreased since 1987, when the age-standardized
indices suggested that cohabiting women were 5.1 as likely as others to have an abortion.
However, the decline may be partly due to random error in the measurement of cohabitation
in the general population.

Some 55% of women having abortions in 1994-1995 have had at least one live birth. When
age is taken into account, women who have had a child are substantially more likely than
others to have an abortion (index values of 1.2-1.5 vs. 0.8). As in 1987, the highest age-
standardized index is found among women who have had four or more births. In all, 72% of
abortion patients who have given birth are unmarried, and 48% of unmarried abortion
patients have borne children (not shown).

For 55% of respondents, this abortion was their first; 7% had had three or more abortions (not shown). In 1987, 57% had not had an abortion before, and 5% had had at least three. The principal reason for the continuing long-term increase in the proportion of abortion patients who have had prior abortions is that with each year since the procedure was legalized, a larger proportion of women in the population have had a first abortion.⁷ The proportion of abortion patients who have had a previous abortion reaches 60% among women 30 and older, who have had more years of exposure to the risk of a first abortion than have younger women.

Protestants account for 37% of abortion patients, but for 54% of the general population of women 18-44, as measured in five 1993-1995 Gallup polls combined;⁸ the resulting age-standardized index is 0.7. The age-standardized abortion rates for Jewish and Catholic women are close to the rate for all women. Women who claim no religious identification appear to have abortions at about four times the rate of women who name a religion.**** None of these rates have changed noticeably since 1987 except the rate for Jewish women, which is unstable because the sample of Jewish women in the Gallup polls and the proportion of the population who are Jewish are small. Among women of "other" religions, the index is 0.8 for 1994-1995, down from 2.0 for 1987. The apparent change may be attributable to differences in the data used for the national comparison: The proportion of women who named a religion classified as "other" was only 2% in the 1982 NSFG, which was used for the 1987 comparisons, but was 8% in the 1993-1995 Gallup polls.

To further explore the difference between the abortion rates of Protestants and Catholics, we calculated the indices after excluding nonwhites and Hispanics, who have high abortions rates. As expected, this exclusion reduced the abortion rate of both Protestants and Catholics, but the difference between the religious groups changed little; the age-standardized rate for Catholic women is 29% higher than that for Protestants (0.6 vs. 0.5). The same pattern was found in 1987.

The questionnaire asked whether the respondent considered herself a "born-again Christian or Evangelical Christian"; this question was taken from a Gallup poll so that comparative data would be available. The proportion responding affirmatively represented a slight increase from 1987 (18% vs. 16%). According to the Gallup polls, 46% of all women 18-44 consider themselves born-again or Evangelical Christians,†so the abortion rate among this group is much below the rate for other women (indices of 0.4 and 1.5, respectively).

The distribution of abortion patients by educational attainment is similar to that of women in the population, with the difference that women with some college but not a bachelor's degree are overrepresented among abortion patients, while college graduates are slightly underrepresented. The age-standardized index, which includes only women aged 20-44, also shows women with some college education to be slightly more likely than others to have an abortion. Among abortion patients aged 20 and older, 57% have attended college or have some postsecondary education.

Women's distribution by level of education as found in the survey differs markedly from the distributions reported by state health departments and published by the National Center for Health Statistics (NCHS). In 1988, the most recent year for which NCHS data are available, 54% of women having abortions in an 11-state area had a high school diploma but no further schooling;⁹ in our survey, the proportion with this level of education was 30%. The NCHS reported about the same proportion of college graduates as our survey (35%), while the

proportions in other categories were lower. If the NCHS reports are accurate, women who completed their education with a high school diploma have a much higher abortion rate than women of any other educational level.

A higher proportion of abortion patients than of all women 15-44 are enrolled in school (30% vs. 25%). When age is adjusted for and women younger than 20 are omitted, enrolled women are 15% more likely to have an abortion than are women not enrolled in school. Among teenagers, the relationship is reversed (not shown): For those aged 15-17, the abortion index is 5.0 among women who have left school and 0.7 among enrolled women; for 18-19-year-olds, the index values are 2.4 and 1.9, respectively. The abortion index for women aged 20 and older who are in school fell from 1.5 to 1.1 between 1987 and 1994-1995.

Although in 1987 employed women had a higher abortion rate than those not working, this was no longer the case in 1994-1995. In the latest survey, 66% of abortion patients were employed, the same proportion as among women in the population.

Women from families with an annual income of less than \$15,000 have a higher abortion rate than do women from families with an income of \$15,000-\$59,999 (indices of 1.9 and 0.9-1.1, respectively), while those with a family income of \$60,000 or more have a lower rate (0.5). Age standardization reduces the income differentials somewhat, but the probability of having an abortion is still three times as high for the lowest income group as for the highest.

The high relative abortion rate of low-income women is reflected in the rate according to Medicaid coverage. Twenty-seven percent of patients say they are covered by Medicaid (although not necessarily for abortion, since only 13 states and the District of Columbia allowed Medicaid to pay for abortion services in 1995), compared with 13% of all U.S. women of reproductive age. The age-standardized indices reveal that women with Medicaid coverage are twice as likely as others to have abortions (1.7 vs. 0.9). The differential is lower than in 1987, when women with Medicaid coverage were nearly three times as likely as others to have abortions.

Some of the differential by Medicaid coverage may be spurious, since most of the states that fund abortions under Medicaid extend eligibility to some low-income pregnant women who would not otherwise qualify, while in the population statistics, such women are not counted as being covered by Medicaid. It is unclear how many women who are not already Medicaid recipients are able to obtain Medicaid coverage for an abortion, but the number may be low.

Women covered by Medicaid have a number of characteristics that may contribute to their relatively high abortion index: They are disproportionately nonwhite, unmarried and poor, all characteristics associated with high abortion rates. And many Medicaid-eligible women are covered by that program because of a prior unplanned pregnancy they carried to term, evidence of difficulty in preventing pregnancy.†

A prior study found that Medicaid funding of abortion made abortion services accessible to women who would otherwise have carried unintended pregnancies to term.¹⁰ We find that in states where Medicaid pays for abortions, women covered by Medicaid have an abortion rate 3.9 times that of women who are not covered, while in states that do not permit Medicaid funding for abortions, Medicaid recipients are 1.6 times as likely as nonrecipients to have abortions. Although the difference may result partly from the ability of some women seeking abortions to qualify for Medicaid because they are pregnant, the magnitude of the difference

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indicates that Medicaid coverage of abortion has an important effect on the ability of poor women to end unwanted pregnancies.

Sixty-six percent of abortion patients intend to have children (including 1% who are unsure). This proportion is lower than that in 1987 (70%), probably because of the older age distribution of the population and of women having abortions. It is higher than the proportion of all women aged 15-44 who intend to have more children (48%), however, reflecting the relatively young age of abortion patients. The age-standardized indices suggest that women who intend to have no more children are 9% more likely to have abortions than are women who intend more children.

As expected, a large majority (89%) of women having abortions live in counties classified by the federal government as metropolitan, and metropolitan women are twice as likely as nonmetropolitan women to have abortions (indices of 1.1 and 0.6, respectively). The comparatively low abortion index of nonmetropolitan women may reflect their difficulty in gaining access to abortion services, which are unavailable in the counties where 85% of nonmetropolitan women reside.¹¹ The limited availability of abortion facilities is indicated by the finding that 43% of the patients surveyed traveled outside their home county for abortion services (not shown). In 1987, by contrast, 39% of abortions took place outside the woman's county of residence.

Contraceptive Use

The patterns of contraceptive use among abortion patients may or may not mirror the use patterns of all women at risk of unintended pregnancy. Each contraceptive method entails a different probability of becoming pregnant, and women's method choice often differs by their socioeconomic and demographic characteristics. Consequently, users of each method may differ in their likelihood of carrying an unexpected pregnancy to term or of having an abortion. For example, women who use only periodic abstinence may, for religious or other reasons, be more likely than users of other methods to carry an unexpected pregnancy to term.

Patterns of contraceptive use among abortion patients therefore result from the combined effect of three factors: the patterns of use among all women, use-failure rates and the likelihood that a woman with an unplanned pregnancy will have an abortion. Changes in the patterns of prior contraceptive use of abortion patients over time can result from changes in any or all of these factors.

Use Status at Conception

Respondents were asked what contraceptive, if any, they had last used before they became pregnant, when they had stopped using that method and how long they had used it. They were considered to have had a contraceptive failure if they were using the method during the month of their last menstrual period. They also were counted as having had a contraceptive failure if they said they had stopped using the method during the month of their last menstrual period, but in response to another question they said they had not stopped using all methods before becoming pregnant. This definition of contraceptive failure, conventionally referred to as "use-failure," means the woman considered herself a method user during the month she became pregnant, although she may not have used a method consistently or correctly.¹²

Overall, 58% of women having abortions have experienced a contraceptive failure; 31% have used a method in the past but were not using one during the month in which they conceived, and 11% have never used any method (Table 2). Even among women younger than 18, 55% were using a method, almost the same proportion as among women 20 and older (57-59%).

Table 2. Percentage distribution of abortion patients, by contraceptive use status during the month in which they became pregnant, according to year and selected characteristics				
Survey year and characteristic	Current user	Prior user	Never-user	Total
1994-1995	57.5	31.2	11.2	100.0
Age-group				
<18	55.4	25.3	19.3	100.0
18-19	58.6	29.1	12.4	100.0
20-29	57.1	33.3	9.7	100.0
>=30	59.0	30.1	10.8	100.0
Poverty status^Y				
0-99%	49.0	34.3	16.7	100.0
100-149%	53.2	33.5	13.3	100.0
150-199%	58.2	31.1	10.7	100.0
>=200%	63.5	28.9	7.6	100.0
Race/ethnicity				
White ^Y	67.0	27.2	5.8	100.0
Black ^Y	52.0	36.1	11.9	100.0
Hispanic	44.7	34.3	21.0	100.0
Other	54.2	28.6	17.1	100.0
1987	51.3	39.7	9.0	100.0
Age-group				
<18	39.4	33.9	26.7	100.0
18-19	48.8	39.8	11.4	100.0
20-29	51.9	41.9	6.2	100.0

>=30	58.8	36.6	4.6	100.0
Poverty status^Y				
0-99%	43.0	44.2	12.7	100.0
100-149%	48.9	43.0	8.0	100.0
150-199%	52.5	40.2	7.3	100.0
>=200%	57.1	35.6	7.4	100.0
Race/ethnicity				
White	57.6	36.1	6.2	100.0
Black	41.8	47.7	10.5	100.0
Hispanic	42.1	41.2	16.7	100.0
Other	53.7	31.9	14.4	100.0
^Y Poverty status is the woman's annual family income expressed as a proportion of the federally designated poverty level for the year in which she was interviewed. The designated level was \$12,320 for a family of four in 1994 and \$ 12,590 for a family of four in 1995. ^y Excluding Hispanics. <i>Source: 1987 data--See reference 2.</i>				

According to the 1988 NSFG, 90% of women at risk of unintended pregnancy are using a contraceptive method and 10% are not.¹³ The abortion indices for current users and nonusers are therefore 0.6 and 4.3, respectively, indicating that women using any method are only about 15% as likely to have an abortion as are women using no method. In other words, even though contraceptive use is often imperfect, it reduces the probability of having an abortion by about 85%.

Poverty status is strongly associated with contraceptive use; 64% of the women whose family income is at least twice the federal poverty level were using a method, compared with 49% of those with an income under the poverty level. Of the racial and ethnic groups, white non-Hispanic women are the most likely to have been using a method (67%), while Hispanic women are the least likely (45%).

The proportion of abortions resulting from contraceptive failure (58%) represents an increase of 12% from 51% in 1987. The increase occurred entirely among women younger than 30 and was greatest among teenagers. While contraceptive use differed sharply by age in 1987, these differences had almost disappeared by 1994-1995. The increase in use occurred equally among all poverty-status groups and among white and black women. Little change occurred, however, among Hispanics and women of races other than white and black.

Both educational attainment and employment status were positively associated with contraceptive use at the time of conception among abortion patients in 1987 and in 1994-1995 (not shown). Of the religious groups, Protestants are the most likely to have been using

a method (60%), while Catholics are the least likely (56%). Among women who became pregnant while using a method, 56% had been using the method for 12 months or less.

Prior Use

Of the 42% of women who were not using a method when they became pregnant, 74% (or 31% of the entire sample) had used one at some time. The majority of prior contraceptive users had most recently relied on either the pill (55%) or the condom (29%). This represents an important shift since 1987, when 74% of prior users had taken the pill and 22% had used the condom.

The women surveyed in 1994-1995 had become pregnant within a fairly short time after discontinuing method use: 32% within the first month and 59% within three months. Among those surveyed in 1987, only 18% had become pregnant within the first month. Additionally, prior users of the pill or the condom seem to have become pregnant more quickly after stopping use than had their counterparts in 1987. In 1994-1995, 53% of prior pill users and 76% of prior condom users became pregnant within three months of stopping use; by comparison, the proportions in 1987 were 44% and 69%, respectively (not shown).

Never-Use

As might be expected, the proportion of abortion patients who have never used any contraceptive method is highest among women younger than 18 (19%); only 10-11% of those aged 20 and older have never used a method. And abortion patients in the two lowest income groups are far more likely to have never used a contraceptive method than are those in higher income groups (13-17% vs. 8-11%).

The proportion who are never-users declines from 21% of Hispanics and 17% of those of races other than white and black to 12% among blacks and 6% among whites. The relatively high proportion of never-users among Hispanic women and those of other races may reflect a concentration of immigrants from cultures where contraceptive prevalence is lower than in the United States. For example, 26% of women who completed the questionnaire in Spanish (presumably the most recent immigrants) had never used a method, compared with 18% of Hispanics who preferred the English version of the questionnaire. Only 8% of Protestants have never used a method, compared with 13% of Catholics (not shown).

Between 1987 and 1994-1995, the proportion of never-users declined markedly among women younger than 18, but increased among women aged 20 and older. Women who completed the questionnaire in Spanish were much older, on average, than other women (only 8% were teenagers, compared with 23% of women who completed the questionnaire in English); these women may in part account for the increase in the proportion of older women who have never used a method. The proportion of women who have never used a contraceptive also increased among the lowest income group (from 13% to 17%) and among those at 100-149% of the poverty level (from 8% to 13%).

Multivariate Analyses

Many of the observed subgroup differences in contraceptive use may reflect confounding of the abortion patients' demographic and socioeconomic characteristics. For example, racial and ethnic differences in the proportion of abortion patients who were using a method when

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they became pregnant may reflect different poverty-status distributions among racial and ethnic groups. We therefore constructed logistic regression models to identify the variables most strongly associated with having been a method user at conception and with never having used any method.

Table 3 (page 146) shows that with other variables controlled, women aged 20 and older are considerably less likely than those younger than 18 to have used a contraceptive at the time of conception (odds ratios of 0.6). The 1988 NSFG found that among women at risk of unintended pregnancy, teenagers were slightly less likely than older women to be using a contraceptive.¹⁴ Since teenagers tend to use less effective methods than older women,¹⁵ teenagers who were using a method are overrepresented among abortion patients.

Table 3. Odds ratios describing the association of abortion patients' characteristics with contraceptive use during the month of conception and with never-use of contraceptives		
Characteristic	Used	Never used
Age-group		
<18	1.000	1.000
18-19	0.797	0.776
20-29	0.618*	0.747*
>=30	0.605*	0.968
Race/ethnicity		
White or other	1.000	1.000
Black	0.606*	1.560*
Hispanic	0.559*	2.230*
Poverty status		
<100%	1.000	1.000
100-149%	1.140	0.829
150-199%	1.227*	0.647*
>=200%	1.328*	0.571*
Marital status		
Never-married	1.000	1.000
Married	1.093	0.811
Formerly married	0.960	0.892

Education		
<H.S.	1.000	1.000
H.S. graduate	1.323*	0.748*
Some college	1.890*	0.416*
>=college	2.179*	0.415*
Religion		
Protestant	1.000	1.000
Catholic	0.957	1.397*
Jewish	0.787	0.700
Other/none	0.983	1.422*
Employed		
Yes	1.000	1.000
No	0.864*	1.371*
Intends more children		
Yes	1.000	1.000
No	1.181*	0.906
*p<.03. A significance level of .03 was chosen as a more conservative test than .05 to allow for possible increased variance due to clustering, weighting and imputation of data.		

Compared with white women and those of other races, blacks and Hispanics are less likely to have used a method (odds ratio of 0.6 for each). Higher economic status, more education, being employed and not wanting more children are positively associated with contraceptive use during the month the conception occurred.

Women aged 20-29 are significantly less likely than the youngest women to have never used a method (odds ratio of 0.7). Blacks and Hispanics are more likely than other women to have never used a method (1.6 and 2.2, respectively); of the variables included, Hispanic origin is most strongly associated with lack of contraceptive experience. The odds that a woman has never used contraceptives decrease as income and educational attainment increase. Catholics and women without a religious identification (or followers of "other" religions) are more likely than Protestants never to have used contraceptives (odds ratio of 1.4 in each case). Women who are not employed in a paid job are more likely never to have used contraceptives than those who are employed (1.4).

Method Used at Conception

Table 4 shows that among abortion patients who were using a method during the month they became pregnant, the condom was the method most commonly used. (The table lists the methods in decreasing order of effectiveness. Women who reported use of more than one method are assigned only to the most effective one; for example, a woman who reported use of both the pill and the condom would be classified as having used the pill.) Of all abortion patients surveyed in 1994-1995, 32% had been using the condom, 12% the pill, 6% withdrawal, 2% periodic abstinence and 1% or fewer each of the other methods. (Written-in responses indicated that some of the pregnancies categorized as injectable failures occurred among women who had intended to continue using the method but were unable to obtain the injection by the required date.)

Table 4. Percentage distribution of abortion patients by contraceptive method used at time of conception, according to year		
Method	1994-1995	1987
Sterilization	0.2	0.2
Implant	0.1	na
IUD	0.1	0.3
Injectable	0.5	na
Pill	11.7	13.3
Condom	32.4	14.8
Female condom	0.2	na
Diaphragm	1.1	5.2
Sponge	1.0	4.7
Foam	0.9	2.0
Suppository	0.9	1.3
Periodic abstinence	2.3	3.8
Withdrawal	5.9	5.7
Other	0.2	0.1
None	42.5	48.7
Total	100.0	100.0

Source: 1987 data--unpublished tabulations from the 1987 abortion patient survey (see reference 2).

The distribution of women by method use in 1994-1995 is sharply different from that in 1987, when only 15% had been using the condom. While reliance on the condom increased

among abortion patients, use of almost all other methods decreased; the diaphragm and sponge saw particularly sharp declines (from 5% to 1%).

To check whether the increase in condom use reflects greater use of condoms at the same time as another method (such as a spermicide), we tabulated the number of respondents who indicated that they had used multiple methods. Among condom users, 46% also checked another method in 1987, compared with only 31% in 1994-1995. Thus, the results suggest a switch to condom use rather than the use of condoms in addition to other methods. Of course, this may not accurately reflect trends in multiple use in the population generally, since women who used the condom together with another method to avoid infection with the human immunodeficiency virus or other sexually transmitted diseases would be less likely to experience an unintended pregnancy and abortion.

Among the women who experienced contraceptive failure, the methods used differ little among the racial or ethnic groups (Table 5). The largest differences are that black women are more likely than nonblack and Hispanic women to have used the condom and less likely to have used withdrawal. Age differences are marked: Whereas 76% of women younger than 18 had used condoms, only 49% of women 30 or older had used this method. Pill use peaked (at 25%) among women aged 20-29, while use of "other" methods (mainly the diaphragm, sponge, spermicides and periodic abstinence) increased sharply with age, from 1% of women younger than 18 to 24% of those 30 and older. Possibly because age is correlated with income, the proportion who used other methods also increased as family income as a proportion of the poverty level rose. Otherwise, there is little association of method used with poverty status.

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Table 5. Percentage distribution of abortion patients who were using a contraceptive a according to selected characteristics

Year and method	Total	Race/ethnicity			Age-group			
		White/ other	Black	Hispanic	<18	18-19	20-29	>=30
1994-1995								
Long-acting	1.5	1.2	1.5	2.2	0.3	1.3	1.5	2.0
Pill	20.3	19.0	21.6	23.0	11.0	16.2	24.8	16.1
Condom	56.6	55.5	61.2	53.2	76.0	64.6	54.9	48.9
Withdrawal	10.3	12.1	6.1	10.5	11.3	14.5	9.7	9.2
Other	11.3	12.1	9.6	11.0	1.4	3.4	9.0	23.7

1987								
Long-acting	1.0	0.8	0.8	2.1	0.0	0.0	0.8	2.5
Pill	26.0	20.9	39.5	30.9	18.3	29.1	31.2	14.0
Condom	28.7	31.4	23.1	22.7	47.4	34.3	25.2	26.8
Withdrawal	11.1	12.0	7.6	12.4	29.4	20.4	8.8	4.1
Other	33.2	34.9	29.0	31.9	5.0	16.2	34.1	52.7
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

†Excluding Hispanics. ‡Sterilization, implant, injectable and IUD. Source: 1987 data--unp survey (see reference 2).

Between 1987 and 1994-1995, condom use among abortion patients who were using a method when they became pregnant increased dramatically among all women, regardless of race, ethnicity, age or poverty status; the increase was greatest among black and Hispanic women. In the same time period, pill use declined among abortion patients who had a contraceptive failure. This decline occurred primarily among blacks and Hispanics, but substantial decreases also took place among women of all ages except those 30 and older, and among those of all income levels except the highest.

The dramatic increase in condom use among teenage abortion patients was accompanied by a large decrease in the proportion using withdrawal. Among those younger than 18, 29% had been using withdrawal and 47% had been using the condom in 1987, while in 1994 -1995, only 11% were using withdrawal and 76% relied on condoms. Among women 20 and older, the increase in condom use coincided with a drop of 25 percentage points or more in the use of "other" methods.

Discussion

The risk of unintended pregnancy leading to abortion varies widely among demographic subgroups. The factors associated with high risk are relatively young age (18-24), being separated or divorced, cohabiting while unmarried, being Hispanic or of a minority race, having a low income, being covered by Medicaid and having had four or more births. Factors that are associated with low abortion rates include being a born-again or Evangelical Christian, being aged 35 or older, having high income, living in a nonmetropolitan county, being married and identifying with a religion other than Catholicism.

With the exception of cohabiting, the characteristics associated with high abortion rates suggest a lack of financial and social resources and, perhaps, a lack of control over one's life. Cohabiting women have sexual intercourse more frequently than do married women,¹⁶ and they may be ambivalent about having children.

Identifying with a religion, on the other hand, suggests integration into a community that provides support and limits on behavior, as well as belief in a doctrine that probably

discourages abortion and sexual activity outside marriage. Being a born-again or Evangelical Christian is associated with a relatively low probability of having an abortion, but even so, 18% of abortion patients are born-again or Evangelical Christians. The causal relationship is not clear, however, since the characteristics that predispose a woman against sexual risk-taking may also predispose her to be born-again or to be attracted to Evangelical religious groups. The surprise, since Catholic dogma is more visibly opposed to abortion than is that of most other religions, is that identification as a Catholic does not result in a low relative abortion rate. One can speculate that the reason might be that Catholics use less effective methods of contraception, are more opposed to childbearing outside marriage or are concentrated in cities and geographic areas with high abortion rates.

Women in nonmetropolitan counties often live in small communities with more effective norms against sexual risk-taking and abortion. This and the relative inaccessibility of abortion services outside metropolitan areas may account for their low abortion rate.

The abortion indices for a number of subgroups have changed since 1987. As noted earlier, some of the difference could be associated with shifts in contraceptive behavior. Another factor may be increased acceptance of childbearing outside marriage. Among teenagers, for example, the decline in abortions was accompanied until 1991 by an increase in nonmarital childbearing. Similarly, the number of abortions obtained by women with no children has decreased, while the relative number among women with two children has gone up. These changes are consistent with the hypothesis that unmarried women are increasingly willing to carry pregnancies to term unless they already have one or two children.

Hispanic women's rising relative abortion rate suggests a need for further research to both confirm the finding and explore the reasons. One can hypothesize that as young Hispanic women become acculturated, they initiate sexual activity at an earlier age and experience more unintended pregnancies. Also, new immigrants may include women with children who wish to terminate childbearing or space their births and turn to abortion because they are unaccustomed to using modern contraceptive methods or have limited access to family planning services.

The observed increase in the proportion of abortion patients who were using a contraceptive method during the month they became pregnant and the shift in methods used could have been affected by changes in the relative effectiveness with which the various methods are used or in the proportions of unintended pregnancies terminated by abortion; however, shifts of this magnitude probably reflect changes in contraceptive use patterns in the population. Data from the 1990 NSFG telephone reinterview survey showed similar patterns of increased condom use among 15-19-year-old, black, never-married, less-educated and low-income women, and decreased pill use among 15-17-year-old, black, never-married and low-income women.¹⁷

Thus, couples appear to have heard the message that they should use condoms to prevent infection with the human immunodeficiency virus and other sexually transmitted diseases. Such a change could increase the unintended pregnancy rate if women switch from the pill or other effective methods, but judging from women having abortions, this has not happened. Among abortion patients, most of the additional condom users replaced women using other barrier methods or no method at all, while the drop in pill users was small.

These findings could indicate that the decrease in the national abortion rate evident in 1992

may have resulted, at least in part, from fewer unintended pregnancies due to greater contraceptive use and net use of more effective methods.¹⁸ In particular, the reduced proportion of nonusers and withdrawal users among teenagers could account for some of the fall in the abortion rate among this age-group if the experience of abortion patients reflects that of the population generally. Similarly, the shift from pill to condom use among black women could help account for the relative increase in the abortion rate of this group.

To further lower the abortion rate, the focus should continue to be on reducing the number of couples who use no contraceptive method at all. Most of those who were not using a method had used one in the past and conceived within a very short period after discontinuing use. Thus, it is very important for couples to avoid lapses in method use and to immediately adopt another method when they discontinue one.

Next in importance would be to improve the effectiveness with which condoms are used, since one-third of abortion patients experienced the failure of this method. Because most of these failures probably resulted from inconsistent use, the need for protection at every act of intercourse should be stressed.

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*For each item requiring imputation, correlations and cross-tabulations were used to identify the variables most strongly associated with it. Respondents were sorted according to these variables in the order of the strength of the item's association with the variable to be imputed, so that similar cases were adjacent to one another in the file. A missing value was then replaced by the value of the preceding case in the file.

**Unpublished tables showing adjusted characteristics of abortion patients for 1989-1991 are available from the authors. For a description of the adjustments made to CDC data, see reference 1.

***For a mathematical proof that the ratio of these proportions is the same as the ratio of the subgroup's abortion rate to the overall abortion rate, see reference 2, p. 162.

****The Gallup interview asks, "What is your religious preference--Protestant, Roman Catholic, Jewish or an Orthodox religion such as the Greek or Russian Orthodox Church?" Our questionnaire asked, "Are you Protestant, Roman Catholic, Jewish or something else?" Answer categories included "Other (specify)" and "None." Some Gallup poll respondents may give the religion in which they were raised even if they are no longer affiliated, while women in an abortion facility may be more likely to say they have no religion. In either case, the abortion index for women with no affiliation would be overestimated, while the indices for those identified with a religion would be underestimated.

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‡The Gallup question combines "born-again" with "Evangelical," a term used by some mainstream Protestant denominations. In a 1993 experiment, Gallup found that the number of positive responses was reduced by 34% when "Evangelical" was omitted from the question. Thus, about 30% of women 18-44 consider themselves born-again Christians. (See: L. McAneny and L. Saad, "Strong Ties Between Religious Commitment and Abortion Views," *Gallup Poll Monthly*, Apr. 1993, pp. 35-43.)

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Unintended Pregnancy in the United States

By Stanley K. Henshaw

Context: Current debates on how to reduce the high U.S. abortion rate often fail to take into account the role of unintended pregnancy, an important determinant of abortion.

Methods: Data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, are used to estimate 1994 rates and percentages of unintended birth and pregnancy and the proportion of women who have experienced an unintended birth, an abortion or both. In addition, estimates are made of the proportion of women who will have had an abortion by age 45.

Results: Excluding miscarriages, 49% of the pregnancies concluding in 1994 were unintended; 54% of these ended in abortion. Forty-eight percent of women aged 15-44 in 1994 had had at least one unplanned pregnancy sometime in their lives; 28% had had one or more unplanned births, 30% had had one or more abortions and 11% had had both. At 1994 rates, women can expect to have 1.42 unintended pregnancies by the time they are 45, and at 1992 rates, 43% of women will have had an abortion. Between 1987 and 1994, the unintended pregnancy rate declined by 16%, from 54 to 45 per 1,000 women of reproductive age. The proportion of unplanned pregnancies that ended in abortion increased among women aged 20 and older, but decreased among teenagers, who are now more likely than older women to continue their unplanned pregnancies. The unintended pregnancy rate was highest among women who were aged 18-24, unmarried, low-income, black or Hispanic.

Conclusion: Rates of unintended pregnancy have declined, probably as a result of higher contraceptive prevalence and use of more effective methods. Efforts to achieve further decreases should focus on reducing risky behavior, promoting the use of effective contraceptive methods and improving the effectiveness with which all methods are used.

Family Planning Perspectives, 1998, 30(1):24-29 & 46

The relatively high rate of unintended pregnancy in the United States¹ has received increasing attention as the immediate cause of both abortion and unplanned birth. For example, the Institute of Medicine recently published a report that summarized the consequences of unintended pregnancies that are carried to term and urged the adoption of a new national goal that all pregnancies be planned.² Improved fertility control would allow women and couples to have children when they feel best prepared socially and financially to assume the responsibilities of parenting.

The most accurate national estimates of unplanned birth have been based on the National Surveys of Family Growth (NSFG), a series of nationally representative surveys that collect detailed reproductive and contraceptive histories and related information from women of reproductive age. A study based on the 1988 NSFG estimated that 57% of pregnancies in 1987 (excluding miscarriages) were unintended; that is, they ended in induced abortion, the woman had wanted no children at that time or she had wanted no more children ever.³ A study of births to ever-married women found that the proportion of births that were unplanned decreased from 38% in 1969-1973 to 32% in 1978-1982, then increased again to 35% in 1984-1988.⁴ Another study comparing the 1982 and 1988 NSFG survey results found that there had been no change in the unintended pregnancy rate between 1982 and 1987, but that the unintended birth rate had increased from 25 per 1,000 women aged 15-44 to 27 per 1,000, while the abortion rate fell by a similar amount.⁵ An earlier study based on the 1982 NSFG concluded that 46% of women aged 15-44 at the time of the survey had experienced one or more unintended pregnancies and that at 1982 rates, 46% would have at least one abortion by age 45.⁶

The publication of data from the 1995 NSFG⁷ provides information on the intendedness of births during the five years preceding the 1995 survey interviews, and can be used as the basis of an updated report on unintended pregnancy. In this article, we assess the prevalence of unintended pregnancy during this period, the changes from 1987 to 1994 and the effect of changes in unintended pregnancy rates on rates of abortion and unplanned birth.

Data and Methodology

Data from the 1995 NSFG and from other sources are used to present estimates, for 1994, of the percentage of births and pregnancies that were unintended, the intended and unintended pregnancy rates, and the proportion of women who have ever had an unintended birth, an abortion or both. In addition, we have calculated the proportion of women who, at 1992 rates, will have had an abortion by age 45. For this analysis, unintended pregnancies were estimated as the sum of abortions and of births resulting from pregnancies reported as having been unintended.

Births

The most recent national data on the planning status of births come from the NSFG, a periodic fertility survey. In addition to the 1995 survey, we also use data from NSFGs conducted in 1982 and 1988.

The 1995 NSFG interviewed a nationally representative probability sample of 10,847 civilian women aged 15-44.⁸ Interviews were conducted between January and October 1995 and included questions on the planning status of each pregnancy experienced by a respondent. Following the NSFG definition, births were categorized as unplanned if the woman had been practicing contraception when she became pregnant, if she had not wanted to become pregnant until a later time or if she had wanted no more children ever. The pregnancy was considered intended if the woman had not been practicing contraception and reported that she had not cared whether she became pregnant. The small number of births for which intention status was undetermined (0.3%) were distributed proportionally.

This information was used to determine the proportion of unplanned births among NSFG respondents in the five years preceding the interview. We chose the five-year period to ensure that the sample size would be large enough to yield a stable proportion. We estimated

the number of unplanned births in the United States by multiplying the resulting proportion with the number of births reported in 1994 by the National Center for Health Statistics (NCHS).⁹

We also estimated unplanned births for 1994 according to the mothers' age, marital status, poverty status, race, ethnicity and contraceptive use during the month of conception. Since the number of births by poverty status is not published by the NCHS, we used the poverty distribution of births, as tabulated from the NSFG. Births to unmarried women are reported by the NCHS, but we used NSFG tabulations to further categorize these women as formerly married or never-married.

For 1981 and 1987, the proportions of unplanned births were taken from published 1982 and 1988 NSFG results¹⁰ and applied to the numbers of births in 1981 and 1987.¹¹ While the NSFG coded the woman as married or unmarried for each birth, it did not include a category for formerly married women. For this reason, we were unable to calculate marital status for 1981.

Finally, using the 1995 NSFG data, we estimated the proportion of U.S. women in 1994 who had ever had an unplanned birth. In the interests of simplicity and comparability with other published data, the results for all analyses are presented according to the age and marital status of the woman at the time of the birth or abortion, rather than her age and marital status at the time of conception. Similarly, the year shown is the year of pregnancy outcome, not the year of conception.

Abortions

In calculating the number of unintended* pregnancies, it was assumed that all pregnancies ending in abortion were unwanted, although a small proportion of abortions may have occurred among initially wanted pregnancies. This may have happened for any number of reasons, including health problems experienced by the woman or the fetus or changes in the woman's circumstances, sometimes resulting from the loss of her partner or lack of support.¹²

To calculate the number of unintended pregnancies in 1994, we needed an estimate of the total number of abortions that occurred during the year and data on the characteristics of women who had abortions. The total number of abortions performed nationally is compiled through periodic surveys of abortion providers conducted by The Alan Guttmacher Institute.¹³ However, this provided abortion estimates only through 1992, the most recent year covered by the surveys. For 1993 and 1994, we projected totals from trends in the number of abortions in published and unpublished reports from state health statistics agencies. We used information only from states with consistent data collection procedures in the two adjacent years (42 states and the District of Columbia to project 1993 totals from the 1992 data, and 43 states and the District of Columbia to project 1994 totals from the 1993 data).

The age, marital status, race and ethnicity of women who had had abortions were based on percentage distributions compiled from state health department reports by the Centers for Disease Control and Prevention (CDC),¹⁴ with adjustments for year-to-year changes in the reporting states.¹⁵ For 1994, we separated unmarried women who had had abortions into subcategories of never-married and formerly married women and derived the distribution of

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abortions by women's poverty status according to data from a 1994-1995 national survey of 9,985 abortion patients.¹⁵ For 1987, we took the distribution of abortions by marital status from a similar survey of 9,480 abortion patients in that year.¹⁶

Because abortions are underreported in population surveys,¹⁷ we decided not to use NFSG data on the number of women in each age-group who had ever had an abortion, a procedure that would have resulted in a serious underestimate. Instead, we made estimates from national abortion statistics, a complicated task since a woman aged 35 in 1994 could have had an abortion in any year since 1973, placing her in a number of possible age-groups. In addition, we wished to avoid counting more than once the many women who have had more than one abortion.

The first step in estimating the number of women in each age-group who have had an abortion was to estimate the number of abortions that occurred in each year according to single year of age. We started with the number of abortions by five-year age-groups (with single-year groupings for teenagers) for each year during 1973-1994, derived from CDC reports with adjustments as described above. To distribute the five-year groups to single years of age, we used microdata tapes compiled by the NCHS for 1980, 1983, 1985, 1986 and 1988-1992.¹⁸ Each tape contains data on more than 280,000 abortions in 12 or more states. We used tabulations of these abortions by single year of age to break down national five-year age-groups into single-year categories. For years lacking an NCHS tape, we interpolated or projected figures.

We also used the tape tabulations to calculate for each year during 1973-1994 the proportion of first-time abortions within each single-year age-group. First, we multiplied the number of abortions by the proportions we had derived from the tapes in order to arrive at an initial estimate for each year of first abortions for each single year of age. We then adjusted the numbers of first abortions in each single-year age category so that the sum for each year was equal to the total number of first abortions previously estimated for that year from CDC data. To estimate the cumulative number of first abortions that took place during 1973-1994 for each age cohort, we added together the number of first abortions that each age-group would have experienced for each year during this period. We then divided this total by the number of women in that age-group in the population in 1994 to arrive at the proportion of U.S. women in each age-group who had ever had an abortion.

Our estimates of the number of first abortions are subject to several possible sources of error: The states included in the NCHS tapes may not have been completely representative of all women having abortions; some women may not have reported their prior abortions to the abortion provider; some of the women who had first abortions died before 1994 and should not have been counted; and some immigrants may have had abortions before coming to the United States.¹⁹ Nevertheless, the results provide an approximate picture of the past abortion experience of U.S. women since the 1973 *Roe v. Wade* decision.

Unintended Pregnancy

We estimated the proportion of women who have ever had an unintended pregnancy by first adding the number of women who had had an unplanned birth to the number who had had an abortion, and then subtracting those who were counted twice because they had had both an unplanned birth and an abortion. Tabulations of the NSFG indicate that the proportion of women who have had an unintended birth and also reported having had an abortion ranged from 9% among women aged 15-19 to 28% among women aged 30-34. Since comparisons

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with national data indicate that the actual number of abortions experienced is about 56% higher than the number reported in the NSFG for the period 1976-1994,¹⁸ we used this figure as a correction factor and adjusted the proportion experiencing both unintended birth and abortion upward for each age-group. Since the rate of abortion underreporting was the same for women younger than 35 and those aged 35-44, we used the same correction factor in all age-groups.¹⁹

Miscarriages

Except where otherwise specified, we excluded miscarriages from all calculations of the number of pregnancies and of pregnancy rates. With miscarriages omitted, the proportion of unintended pregnancies that ended in abortion reflects actual decisions to terminate or continue pregnancies. In addition, it assures that all tables in this article are consistent, since it would be difficult to calculate the proportion of women who have ever had an unintended pregnancy while at the same time taking into account the overlap between women who have had unintended pregnancies that ended in miscarriage, birth and abortion. (However, the number of miscarriages after 6-7 weeks of pregnancy--the point at which miscarriages are likely to be noted by the woman--can be estimated by adding 20% of births to 10% of abortions.²⁰ Miscarriages may also be estimated using NSFG data.²¹)

Results

Rates and Outcomes

Approximately 3.95 million births and 1.43 million abortions occurred in 1994, for a total of 5.38 million pregnancies, not including miscarriages. (Use of the estimation procedure mentioned above produces an estimated 930,000 miscarriages during the year as well.) The largest number of pregnancies occurred among women aged 20-29, among currently married women, among those with an income 200% or more of the federal poverty level, and among white and non-Hispanic women (Table 1).

Table 1. Estimated number of pregnancies (excluding miscarriages), percentage distribution by intention, and selected measures of unintended pregnancy, all by characteristic, 1994

Characteristic	No. of pregnancies	% distribution of pregnancies				% of births that were unintended	% of pregnancies that were unintended
		Intended births	Unintended births	Abortions	Total		
Total	5,383,800	50.8	23.0	26.6	100.0	30.8	49.2
Age at outcome							
<15Y	25,100	18.3	33.2	48.5	100.0	64.5	81.7
15-19	781,900	22.0	42.7	35.3	100.0	66.0	78.0
15-17	306,100	17.3	46.5	36.2	100.0	72.9	82.7
18-19	475,800	25.0	40.2	34.8	100.0	61.7	75.0
20-24	1,479,500	41.5	26.2	32.3	100.0	38.7	58.5
25-29	1,405,200	60.3	17.2	22.5	100.0	22.2	39.7
30-34	1,111,400	66.9	14.6	18.4	100.0	18.0	33.1
35-39	482,400	59.2	17.9	23.0	100.0	23.2	40.8

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>=40y	98,300	49.3	17.9	32.8	100.0	26.7	50.7
Marital status at outcome							
Currently married§	3,003,900	69.3	19.3	11.3	100.0	21.8	30.7
Formerly married	356,700	37.5	21.8	40.7	100.0	36.8	62.5
Never-married	2,023,100	22.3	31.0	46.7	100.0	58.2	77.7
Poverty status**							
<100%	1,358,000	38.6	31.3	30.1	100.0	44.8	61.4
100-199%	1,292,500	46.8	27.7	25.4	100.0	37.2	53.2
>=200%	2,733,200	58.8	15.9	25.4	100.0	21.3	41.2
Race							
White	3,981,700	57.1	21.2	21.6	100.0	27.1	42.9
Black	1,130,700	27.7	28.6	43.7	100.0	50.8	72.3
Other	271,400	50.0	22.0	28.0	100.0	30.5	50.0
Ethnicity							
Hispanic	900,200	51.4	22.4	26.1	100.0	30.4	48.6
Non-Hispanic	4,483,600	50.7	22.6	26.7	100.0	30.9	49.3
*Pregnancy rates for this category are expressed as per 1,000 women aged 15-44, except for rates is women aged 14. yNumerator for rates is women aged 40 and older; denominator is women. **Percentage of federal poverty level at time of interview. In 1994, the federal poverty level was \$4,748 for a family of four. Note: Intention status of births is based on births in the five years before the 1995 interview.							

During the five years preceding the 1995 NSFG interview, 31% of births were reported as unintended--that is, the woman did not want to have children when she did (21%) or wanted no more births ever (10%). Applying the same proportions to 1994 births, we estimated that 1.22 million births resulted from unintended pregnancies. Adding abortions, there were 2.65 million unintended pregnancies, or 49% of all pregnancies for that year. (If we include an estimated 390,000 miscarriages that would have otherwise ended in abortion or unintended birth, we find that a total of 3.04 million unintended pregnancies occurred during 1994.) Of all pregnancies in 1994 (excluding miscarriages), 23% ended in unintended births and 27% in abortions. Thus, among women who experienced an unintended pregnancy in 1994 (excluding miscarriages), 54% had an abortion and 46% carried the pregnancy to term.

Forty-eight percent of the women who had an unplanned birth had been using a contraceptive method during the month they became pregnant,** as had 58% of those who had abortions (not shown). For all unintended pregnancies combined, slightly more than half (53%) of the women had been using a method. Of the contraceptive users, 58% ended their pregnancies by abortion, compared with 49% of nonusers who had accidental pregnancies. (When the estimated number of unintended pregnancies that ended in miscarriage is included, the percentage of women who were using a method remains at 53%, but among contraceptive users, we estimate that 51% had abortions, 37% had births and 12% had miscarriages; among nonusers, we estimate that 43% had abortions, 44% had births and 13% had miscarriages.)

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Thus, contraceptive users appear to have been more motivated to prevent births than were nonusers, although many nonusers did have abortions.

The proportion of all pregnancies that were unintended varied sharply by age, with teenagers younger than 18 having the highest percentage (82-83%). The proportion decreased with rising age, dropping to 33% among women aged 30-34, and then increased again, reaching 51% among women aged 40 and older. Some 44% of teenagers aged 15-17 ended their unintended pregnancies by abortion, the lowest proportion in any age-group. (The relatively high proportion among women younger than 15 is misleading because it excludes the pregnancies of 14-year-olds that ended in births at age 15. It also excludes pregnancies to 14-year-olds that ended in abortion at age 15, but there are relatively few of these.) The proportion was also relatively low for women aged 18-19 (46%), and was highest among women older than 40 (65%).^{*Y}

The unintended pregnancy rate shows that for every 1,000 women aged 15-44, about 45 had an accidental pregnancy during 1994 (or nearly 5%). Among women aged 15-17, the rate was similar to that for all women. It peaked at 105 per 1,000 among women aged 18-19, then dropped sharply with age. At these rates, a cohort of 100 women will have experienced 142 unintended pregnancies, or about 1.42 per woman, by the time they are 45 (not shown).

The intended pregnancy rate was about the same as the unintended rate (46 per 1,000), having increased from 40 per 1,000 in 1987 and 43 per 1,000 in 1981 (not shown). The age pattern of intended pregnancy, however, was very different from that of unintended pregnancy: Intended pregnancy was much higher than unintended pregnancy among women aged 25-39 and much lower than unintended pregnancy among teenagers. Each year, 1% of all women aged 15-17 had an intended pregnancy.

Among married women, 31% of pregnancies were unintended, compared with 63% among formerly married women and 78% among never-married women. Only 37% of married women who had unintended pregnancies ended them by abortion, compared with 60-65% of unmarried women. The pregnancy rate among never-married women (91 per 1,000) was about the same as that of married women (95 per 1,000). The outcomes of these pregnancies reflect differences in intention status for these groups, however: Almost half of pregnancies among formerly and never-married women ended in abortion (47% and 41%, respectively), compared with only 11% of those among married women.

Women's poverty status (defined as the ratio of family income to the federal definition of poverty)^{*Y} was strongly associated with the unintended pregnancy rate but only weakly associated with the rate of intended pregnancy. Among women in poverty, pregnancies were more likely than among higher income women to be unintended and to end in unplanned births, and were slightly more likely to end in abortions. The overall pregnancy rate declined with increasing income, and this trend resulted mainly from the higher rate of unintended pregnancy among poor women. The proportion of poor women's unintended pregnancies that ended in abortion was similar to the proportion among women living at 100-199% of the poverty level, and was less than that among women whose income was 200% or more of the poverty level.

The differences between white and black women generally paralleled those between high- and low-income women: Compared with white women, black women had a higher pregnancy rate. The higher pregnancy rate for black women resulted from an unintended

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pregnancy rate that was almost three times that of white women. Because black women's unintended pregnancy rate was so high, the proportion of these women's pregnancies that ended in abortion (44%) was much higher than that of white women (22%).

On all measures, women of other races fell between white and black women, usually closer to white women. Hispanic women had a much higher rate of both intended and unintended pregnancy than did non-Hispanic women, but the percentage of unintended pregnancies and births and the distribution of outcomes were almost identical for Hispanic and non-Hispanic women.

Trends

There have been significant changes over time in the frequency of unintended pregnancy and in the resolution of such pregnancies, especially since 1987. Between 1981 and 1987, the unintended pregnancy rate changed little, but from 1987 to 1994, the rate dropped 16%, from 54 per 1,000 to 45 per 1,000 (Table 2). As a result, the rates of both unintended births and abortions fell between 1987 and 1994, but the drop was greater for unintended births (6 per 1,000) than for abortions (3 per 1,000). Consequently, the proportion of unintended pregnancies ended by abortion increased from 50% to 54%.

Table 2. Estimated rates of unintended pregnancies, unintended births and abortions per 1,000 women, age and marital status, and percentage of unintended pregnancies ended by abortion, by characteristic, 1981, 1987 and 1994

Characteristic	Unintended pregnancy			Unintended birth			Abortion			% ended by abortion		
	1981	1987	1994	1981	1987	1994	1981	1987	1994	1981	1987	1994
Total	54.2	53.5	44.7	25.0	26.6	20.9	29.2	26.9	24.1	53.9	50.3	54.0
Age at outcome												
15-19	78.1	79.3	71.1	35.2	37.1	38.9	42.9	42.2	32.2	54.9	53.2	45.3
20-24	93.6	102.7	96.0	42.3	50.2	43.0	51.4	52.5	53.0	54.8	51.1	55.2
25-29	60.6	66.1	58.4	29.3	35.4	25.3	31.3	30.8	33.1	51.6	46.5	56.7
30-34	37.0	37.3	33.1	19.3	19.3	14.6	17.7	17.9	18.4	47.8	48.2	55.7
35-39	15.0	18.8	17.8	5.5	9.0	7.8	9.5	9.8	10.0	63.5	52.2	56.3
>=40*	4.3	5.3	5.0	0.9	2.4	1.8	3.4	2.9	3.2	78.2	54.3	64.7
Marital status at outcome												
Currently married ^Y	u	41.5	29.2	u	29.8	18.4	u	11.7	10.8	u	28.2	37.0
Formerly married	u	54.6	40.4	u	19.0	14.1	u	35.7	26.3	u	65.3	65.1
Never married	u	71.5	70.8	u	23.2	28.2	u	48.2	42.5	u	67.5	60.1

*Numerator for rates is women aged 40 and older; denominator is women aged 40-44. ^YIncludes separated women. Notes: All measures exclude miscarriages. The intention status of births is based on births in the five years before the interviews in 1988 and 1995 and in the four years before the 1982 interview. u=unavailable.

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The changes differed markedly by age-group, especially when teenagers were compared with women aged 20 and older. Between 1981 and 1987, the unintended pregnancy rate and birthrate changed little among teenagers but increased among all women aged 20 and older, except among women aged 30-34. Changes in abortion rates were very small during this period. From 1987 to 1994, the rate of unintended pregnancy fell among all age-groups, although the change was small among women aged 35 and older. Among teenagers, the drop in unintended pregnancy affected only the abortion rate, which fell by 24% (from 42 per 1,000 to 32 per 1,000), while the rate of unintended births actually increased slightly (from 37 per 1,000 to 39 per 1,000). Among all other age-groups, the abortion rate increased slightly or stayed the same, while the rate of unintended births fell significantly as a consequence of the reduced rate of unintended pregnancy. In 1994, teenage women were less likely than women in any other age-group to end an unintended pregnancy by abortion, whereas in earlier periods teenagers have been similar to other women in this respect.

Between 1987 and 1994, currently and formerly married women experienced reductions in unintended pregnancy that were reflected in decreases both in the rate of unintended birth and in that of abortion. Among married women, the proportion of unintended pregnancies that ended in abortion increased from 28% to 37%. Never-married women, on the other hand, reported an increase in unintended births that was approximately equal to the decrease in abortions in this group, and the proportion of unintended pregnancies that ended in abortion declined.

All three income groups experienced a decrease in the proportion of pregnancies that were unintended (not shown).²² The proportion of unintended pregnancies that ended in abortion remained about the same among women in the lowest income group, decreased among those in the middle income group and increased sharply among women in the highest income category.

Lifetime Experiences

Over their lifetime, the proportion of women experiencing an unintended pregnancy is substantial, even when the proportion in any one year is small. Of the women aged 15-44 who were surveyed in the 1995 NFSG, 28% indicated that they had had one or more unplanned births, and based on national abortion statistics, 30% of women had had one or more abortions (Table 3). The probability of having experienced an unplanned birth increased with age, largely because of the increased years of exposure to pregnancy risk. By the time they were 40-44, 38% of the women surveyed had had this experience.

Table 3. Percentage of women who have ever had at least one unplanned birth, abortion or unintended pregnancy, by age-group, 1994

Age	>=1 unplanned births	>=1 abortions*	Both birth and abortion	>=1 unintended pregnancies ^Y
Total	28.4	29.9	10.6	47.7
15-19	6.1	7.0	0.9	12.2
20-24	22.5	26.3	7.4	41.4

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30-34	33.7	40.2	14.8	59.2
35-39	36.6	38.3	14.9	60.0
40-44	38.1	25.0	12.7	50.4
*Since 1973. †Excludes miscarriages.				

Similarly, the probability of having had an abortion also increased with age, rising from 7% among women aged 15-19 to 40% among women aged 30-34. The proportion was lower among women older than 34 because this research did not attempt to include abortions before 1973, when these women experienced their highest-risk years (ages 15-24). Overall, 11% of all women had had both at least one unplanned birth and at least one abortion. Among women in their 30s, this proportion was 15%.

About 48% of all women aged 15-44 had ever had an unintended pregnancy (either an unplanned birth or an abortion, or both). The percentage increased with age, to a high of 60% among women 35-39. Although the percentage was lower among women aged 40-44, this figure may be understated, again because neither legal nor illegal abortions that occurred before 1973 were counted in this estimate.

Although we know how many women in each age-group had already had an unintended pregnancy, we cannot say exactly how many will have one by age 45, because of the difficulties of estimating the proportion of women having a first abortion who have previously had an unplanned birth and, of those having an unplanned birth, the proportion who have had an abortion. However, we were able to make lifetime abortion estimates at 1992 rates, the most recent year for which data were available (Table 4).*§;

Table 4. Abortion rate per 1,000 women and percentage of abortions that were first abortions, and first-abortion and cumulative first-abortion rates, by year, all according to age-group

Age	Abortion rate in 1992	% that were first abortions in 1992	First-abortion rate		Cumulative first-abortion rate*	
			1982	1992	1982	1992
Total	25.9	.530	17.8	13.7	na	na
<15†	7.6	.942	7.8	7.2	7.8	7.2
15-17	23.1	.855	26.0	19.7	85.8	66.4
18-19	53.8	.722	45.4	38.9	176.6	144.1
15-19	35.5	.760	34.1	27.0	176.6	144.1
20-24	56.3	.541	30.3	30.5	328.1	296.5
25-29	33.9	.419	15.7	14.2	406.6	367.5
30-34	19.0	.393	7.1	7.5	442.1	404.8

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35-39	10.4	.405	2.8	4.2	456.1	425.9
40-44 ^y	3.2	.453	0.7	1.4	459.6	433.1
<p>*Number having an abortion by end of specific age-period, per 1,000 women, at current rates. ^yDenominator for rates is women aged 14. ^yNumerator for rates is women aged 40 and older; denominator is women aged 40-44. <i>Note:</i> na=not applicable. <i>Sources:</i> 1982 DATA--See reference 6.</p>						

We estimated the first-abortion rate by applying the 1992 proportion of first abortions for each age-group to the abortion rate for that age-group. The cumulative first-abortion rate indicates the number of women per 1,000, at 1992 rates, who will have had a first abortion by the time they reach the end of the age range. At these rates, 14% of women can expect to have had an abortion before age 20, 37% by age 30 and 43% by age 45.^{y*}

The 1992 cumulative lifetime first-abortion rate was slightly lower than the 1982 cumulative rate (46%),²³ and the rate may be still lower today, since abortion rates fell somewhat between 1992 and 1994. The drop between 1982 and 1992 was almost entirely the result of the lower first-abortion rate among teenagers, which fell by seven percentage points; the first-abortion rate among other age-groups changed by no more than two percentage points.

Discussion

Although it is well known that unintended pregnancy is common in the United States, the statistics presented in this article show just how widespread the experience is: Half of all pregnancies are unintended; 28% of women aged 15-44 have had an unplanned birth and 30% have had an abortion; 60% of women in their 30s have had an unplanned birth or an abortion; and, at 1992 rates, 43% of women will have had an abortion by age 45. Some of the women who are most prone to unintended pregnancy, especially unmarried and low-income women, are those who may have the greatest difficulty caring for an unanticipated child.

In spite of the disruption that can be caused by an unplanned birth, only about half of unintended pregnancies are terminated by abortion. A majority of married women (63%) continue their unintended pregnancies, possibly because they find it easier to accommodate an additional child than do unmarried women. However, 35% of formerly married women and 40% of never-married women also continue their unplanned pregnancies.

Between 1987 and 1994, the rate of unintended pregnancy fell from 54 pregnancies per 1,000 women of reproductive age to 45 per 1,000, a decrease of 16%. A likely explanation for the decline in unintended pregnancy is an increase in widespread and effective contraceptive use. The 1995 NSFG data show that condom use has increased significantly, and that the proportion of contraceptive nonusers among women at risk of unintended pregnancy has gone down.²⁴ Another possible factor is the availability of two new highly effective contraceptives, the implant and the injectable. In part because Medicaid pays for these methods, many of the women who adopted them were at especially high risk of unintended pregnancy--even when they were using other reversible methods. Therefore, use of the new methods may have prevented a disproportionate number of pregnancies.

Overall, the drop in unintended pregnancy between 1987 and 1994 is reflected in decreases

in the rates of both unplanned birth and abortion. Further progress is needed, however. In view of the lower rates of unintended pregnancy in other developed countries,²⁵ such progress should be possible.

Among women aged 20 and older, the reduction in unintended pregnancy resulted in lower rates of unplanned birth. Abortion rates in this group changed little or increased slightly. Thus, the percentage of unintended pregnancies ended by abortion increased, indicating that women and couples had become less willing to accept unplanned births. One reason for the change is that a higher proportion of women in each age-group were not currently married. Among unmarried women, 60-65% resolved unintended pregnancies by abortion, compared with 37% among married women. Of women aged 25-29, the proportion who were currently married and living with their husband fell from 59% in 1987 to 53% in 1994.²⁶ Even within the married group, however, more women ended their unintended pregnancies by abortion in 1994 than did so in 1987. One possible reason may be married couples' increased reliance on the woman's earnings.

The pattern among teenagers is remarkably different. Among women aged 15-19 who had an unwanted pregnancy, the proportion who ended these pregnancies by abortion fell from 53% to 45%. The abortion rate declined 24%, while the rate of unplanned birth did not decline at all--and may have increased slightly. In the absence of data, any explanation of the differences between teenagers and other age-groups is speculative. One hypothesis is that teenagers may have been influenced by antiabortion messages. Other possible reasons are decreased access to abortion services, barriers posed by parental involvement statutes, and use of better contraceptive methods (such as the injectable and implant) by those teenagers who are strongly motivated to avoid childbearing, leaving unplanned pregnancies more concentrated among those less motivated to avoid childbearing.

Whether they end in abortion or unplanned birth, unintended pregnancies come at a cost both to the individuals involved and to the larger society. Reduction of unplanned pregnancy can only be achieved by decreasing risky behavior, promoting the use of effective contraceptive methods and improving the effectiveness with which all methods are used. More research is needed on the best ways to accomplish these goals, but we know that sensible strategies are to improve the accessibility of contraceptive services, to dispel misconceptions about the health risks of contraception and to make emergency contraception easily available and widely known.

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§ The number of immigrants exceeded the number of deaths, resulting in an increase by 3-4% of the number of women in each age cohort between 1980 and 1990.

**Based on NFSG tabulations of births that were conceived after January 1, 1991, and that took place before the interview. For abortion data, see reference 15.

*Y These figures are based on the age of the woman when the pregnancy ended, not her age at conception. Adjustment to age at conception would lower the proportions for women younger than 20 and raise them for women older than 30.

*y In 1994, the federal poverty level was \$17,020 for a family of four.

*§ Information on the proportion of first abortions by age is unavailable for years since 1992. For calculating the lifetime experience of abortion for Table 3, we assumed that the 1993 and 1994 proportions of first abortion were similar to those for 1992, since small errors would have little effect on the results. The cumulative first abortion rate, however, depends entirely on these proportions, which are only accurate for 1992.

Y* In the future, one can expect that for women having abortions at age 35 or older, a lower proportion will be having a first abortion, since a greater proportion of their reproductive lives will have occurred while legal abortion has been available. If we assume that the proportion of first abortions was .35 for women aged 35-39 and .30 for women aged 40-44, the cumulative abortion rate for women aged 45 will be 428 per 1,000, similar to the rate of 433 per 1,000, shown in Table 4.

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Complications of Interval Laparoscopic Tubal Sterilization: Findings From the United States Collaborative Review of Sterilization

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Objective: To estimate the risk of intraoperative or postoperative complications for interval laparoscopic tubal sterilizations.

Methods: We used a prospective, multicenter cohort study of 9475 women who had interval laparoscopic tubal sterilization to calculate the rates of intraoperative or postoperative complications. The relative safety of various methods was assessed by calculating overall complication rates for each major method of tubal occlusion. Method-related complication rates also were calculated and included only complications attributable to a method of occlusion. We used logistic regression to identify independent predictors of one or more complications.

Results: When we used a more restrictive definition of unintended major surgery, the overall rate of complications

went from 1.6 to 0.9 per 100 procedures. There was one life-threatening event and there were no deaths. Complications rates for each of the four major methods of tubal occlusion ranged from 1.17 to 1.95, with no significant differences between them. When complication rates were calculated, the spring clip method had the lowest method-related complication rate (0.47 per 100 procedures), although it was not significantly different from the others. In adjusted analysis, diabetes mellitus (adjusted odds ratio [OR] 4.5; 95% confidence interval [CI] 2.3, 8.8), general anesthesia (OR 3.2; CI 1.6, 6.6), previous abdominal or pelvic surgery (OR 2.0; CI 1.4, 2.9), and obesity (OR 1.7; CI 1.2, 2.6) were independent predictors of one or more complications.

Conclusion: Interval laparoscopic sterilization generally is a safe procedure; serious morbidity is rare. (Obstet Gynecol 2000;96:997-1002. © 2000 by The American College of Obstetricians and Gynecologists.)

From the Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

The U.S. Collaborative Review of Sterilization Working Group: Design, Coordination, and Analysis Center: Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia. Principal Investigator: Herbert B. Peterson, MD; Project Officer: Joyce M. Hughes; Project Associates: Zhisen Xia, PhD, Lynne S. Wilcox, MD, Lisa Ratliff Tylor; Project Consultant: James Trussell, PhD; Data Collection Centers Project Directors: Norman G. Courey, MD, CM, State University of New York at Buffalo, Erie County Medical Center, Buffalo, New York; Philip D. Darney, MD, MSc, University of California, San Francisco, San Francisco, California; Ernst R. Friedrich, MD, Washington University School of Medicine, St. Louis, Missouri; Ralph W. Hale, MD, Roy T. Nakayama, MD, Kapiolani Medical Center, Honolulu, Hawaii; Jaroslav F. Hulka, MD, University of North Carolina School of Medicine, Chapel Hill, North Carolina; Alfred N. Poindexter, MD, Baylor College of Medicine; George M. Ryan, MD, Edwin M. Thorpe, MD, University of Tennessee School of Medicine, Memphis, Tennessee; Gary K. Stewart, MD (deceased), Planned Parenthood of Sacramento, Sacramento, California; Howard A. Zacur, MD, Lucas Blanco, MD, Johns Hopkins University School of Medicine, Baltimore, Maryland.

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Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy

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The complication rate among 282 women undergoing interval tubal sterilization by laparotomy was studied as part of the prospective multicenter Collaborative Review of Sterilization. Using a standard definition of major complications, the overall complication rate was 5.7 per 100 procedures. Women experiencing complications had a significantly lengthened postoperative recovery period before the resumption of normal activities. Important risk factors for complications included diabetes, cigarette smoking, previous abdominal or pelvic surgery, and a history of pelvic inflammatory disease. Women with an initial abdominal incision of 7 cm or longer had three times the complication rate of women with shorter incisions. These results provide objective evidence that, for tubal sterilizations, minilaparotomy (laparotomy with a small abdominal incision) is associated with lower morbidity than is conventional laparotomy. (*Obstet Gynecol* 62:180, 1983)

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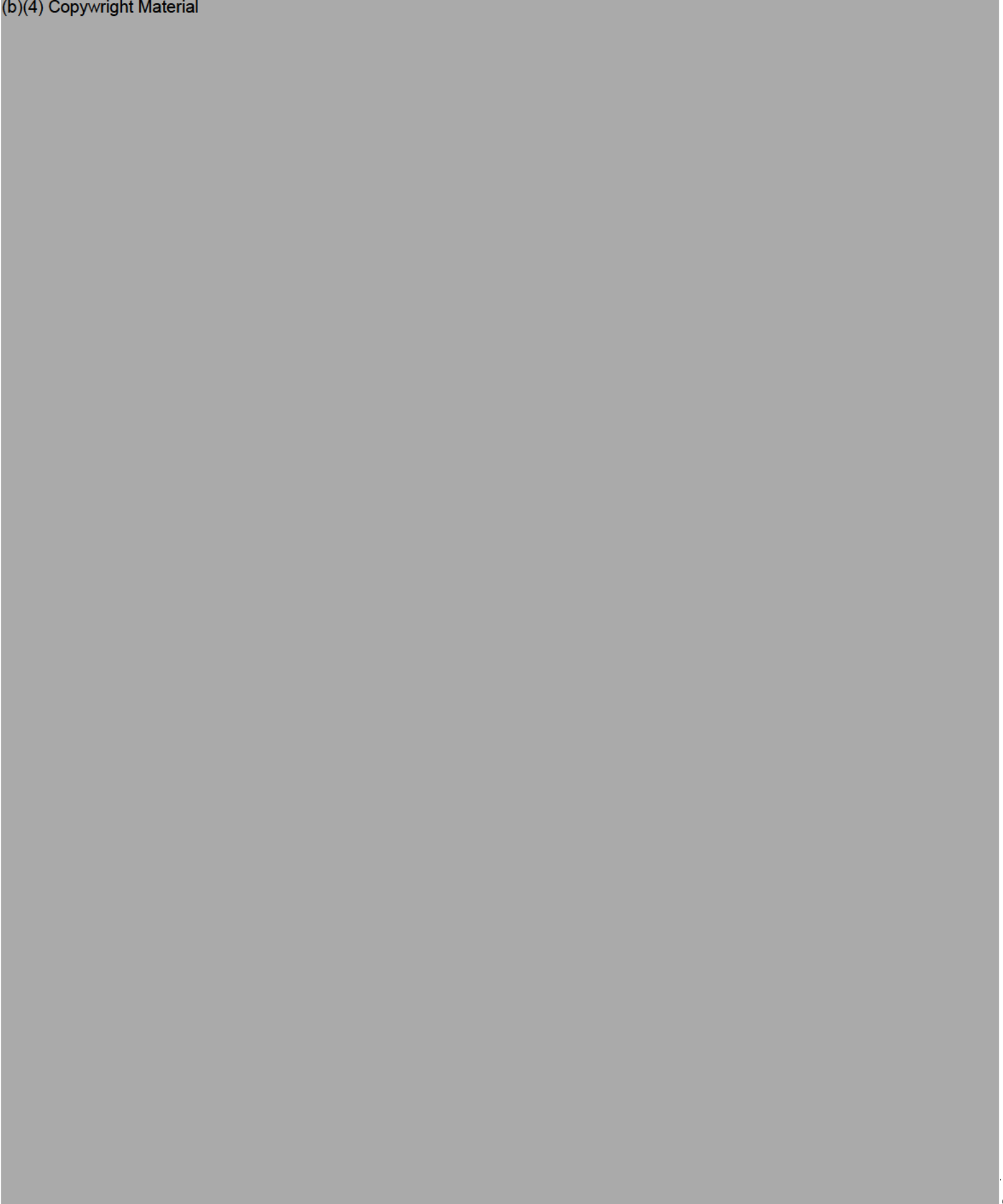
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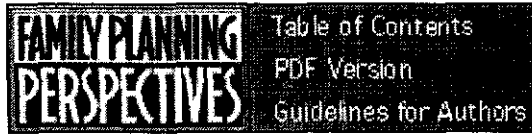


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Tubal Sterilization in the United States, 1994-1996

By Andrea P. MacKay, Burney A. Kieke, Jr., Lisa M. Koonin and Karen Beattie

Context: Although the number and rate of tubal sterilizations, the settings in which they are performed and the characteristics of women obtaining sterilization procedures provide important information on contraceptive practice and trends in the United States, such data have not been collected and tabulated for many years.

Methods: Information on tubal sterilizations from the National Hospital Discharge Survey and the National Survey of Ambulatory Surgery was analyzed to estimate the number and characteristics of women having a tubal sterilization procedure in the United States during the period 1994-1996 and the resulting rates of tubal sterilization. These results were compared with those of previous studies to examine trends in clinical setting, in the timing of the procedure and in patient characteristics.

Results: In 1994-1996, more than two million tubal sterilizations were performed, for an average annual rate of 11.5 per 1,000 women; half were performed postpartum and half were interval procedures (i.e., were unrelated by timing to a pregnancy). All postpartum procedures were performed during inpatient hospital stays, while 96% of interval procedures were outpatient procedures. Postpartum sterilization rates were higher than interval sterilization rates among women 20-29 years of age; interval sterilization procedures were more common than postpartum procedures at ages 35-49. Sterilization rates were highest in the South. For postpartum procedures, private insurance was the expected primary source of payment for 48% and Medicaid was expected to pay for 41%; for interval sterilization procedures, private insurance was the expected primary source of payment for 68% and Medicaid for 24%. 1989, 21(5):209-212.

Conclusions: Outpatient tubal sterilizations and procedures using laparoscopy have increased substantially since the last comprehensive analysis of tubal sterilization in 1987, an indication of the effect of technical advances on the provision of this service. Continued surveillance of both inpatient and outpatient procedures is necessary to monitor the role of tubal sterilization in contraceptive practice.

Family Planning Perspectives; Family Planning Perspectives, 2001, 33(4):161-165

Tubal sterilization is the most commonly used method of birth control in the United States: The 1995 National Survey of Family Growth (NSFG) reported that 28% of all women 15-44 years of age currently practicing contraception relied on tubal sterilization.¹ Tubal sterilization also is a highly effective method for women choosing to permanently terminate their reproductive ability. For example, the Collaborative Review of Sterilization (CREST) study reported a first-year probability of pregnancy of 5.5 pregnancies per 1,000 sterilization procedures and a 10-year cumulative probability of 18.5 per 1,000.²

The number and rate of tubal sterilizations performed, the settings in which they are performed and the characteristics of the women obtaining sterilization procedures provide important information on contraceptive practice and trends to public health programs such as Title X, to the Health Resources and Services Administration and state family planning agencies, and to managed care organizations, health care providers, research institutions and advocacy organizations. Information on trends in sterilization rates contributes to the general knowledge of contraceptive practice in the United States and the role of sterilization within that framework. These data can inform health care programs and providers of shifts in the need for services.

No national reporting system exists to count sterilizations performed in the United States. In the past three decades, a number of studies by the Centers for Disease Control and Prevention (CDC) and EngenderHealth (formerly AVSC International) have attempted to estimate the number of procedures performed each year, by combining data from a variety of sources, including physicians who perform sterilizations, medical facilities where sterilizations are performed and comprehensive national surveys.³

Since 1965, CDC's National Center for Health Statistics (NCHS) has relied on the National Hospital Discharge Survey (NHDS) to collect data each year on inpatient surgical and nonsurgical procedures. In response to the shift of many surgical procedures to outpatient settings, in 1994 NCHS initiated the National Survey of Ambulatory Surgery (NSAS) to augment the NHDS. These two surveys provide the most comprehensive estimates available of tubal sterilizations performed in the United States. We used data from the NHDS and NSAS to estimate the number and rate of tubal sterilizations for 1994 through 1996, as well as the clinical settings, timing of procedures and characteristics of women undergoing tubal sterilization.

Methods

The data sources for this analysis were the 1994, 1995 and 1996 NHDS⁴ and

the 1994, 1995 and 1996 NSAS.⁵ These years represent the most recently available data on all tubal sterilizations in the United States; the NSAS has not been repeated since 1996.

Clinical setting was classified as hospital inpatient (i.e., involving an overnight hospital stay), hospital ambulatory surgery centers (including procedures performed in hospitals as outpatient procedures) or freestanding surgery centers.

Hospital inpatient tubal sterilization discharges were estimated using the NHDS, an annual multistage probability sample of discharges from nonfederal, short-stay hospitals in the United States. Up to seven diagnosis codes and four procedure codes were collected for each patient. Demographic and medical information was obtained either from the face sheets of sampled records or from automated sources.

We estimated the number of outpatient visits for tubal sterilization using the NSAS, a multistage probability sample of ambulatory surgery visits in hospital-based and freestanding ambulatory surgery centers and of outpatient procedures performed in hospitals. (Procedures performed in hospital ambulatory surgery centers included those performed in hospital operating rooms on an outpatient basis.)

The sample universe included surgery centers in noninstitutional, nonfederal, short-stay hospitals and freestanding facilities listed in the 1993 SMG Freestanding Outpatient Surgery Center Database. If a freestanding facility was owned by a hospital but located some distance away, was separately listed in the 1993 SMG Freestanding Outpatient Surgery Center Database and was selected into the NSAS sample from this universe, it was considered a freestanding surgery center. Facilities specializing in abortion, family planning or delivery were excluded from the survey. A maximum of seven diagnostic codes and six procedure codes were collected for each patient.

Tubal sterilization is a permanent method of birth control in which a portion of the fallopian tube is cut and either tied, clipped, cauterized or removed. For this analysis, we defined postpartum tubal sterilizations as procedures that were completed during the same hospital stay as a delivery; interval tubal sterilizations were unrelated by timing to a pregnancy or a delivery. Our analysis is restricted to women aged 20-49.

We identified postpartum tubal sterilizations using International Classification of Disease, Clinical Modification, Ninth Revision (ICD-9-CM)⁶ codes that restricted the case selection to those that matched for a vaginal or cesarean delivery (diagnosis code V27) and tubal sterilization codes (procedure codes 66.2-66.3 or procedure codes 65.6, 66.5, 66.63 or 66.97 and diagnosis code V25.2), and excluded any procedures in which the removal of the fallopian tubes was an integral part of a hysterectomy or a procedure for reasons other

than sterilization. Inpatient interval tubal sterilizations were identified similarly, excluding any matches with delivery codes. Outpatient interval procedures were identified using ICD-9-CM codes; again, we excluded any procedures in which the removal of the fallopian tubes was an integral part of a hysterectomy or a procedure for reasons other than sterilization. Postpartum sterilizations are not routinely performed in outpatient settings, because by definition, they take place less than 48 hours after a delivery.

We categorized type of delivery (vaginal or cesarean) associated with postpartum sterilization procedures from ICD-9-CM procedure codes. We also ascertained the surgical procedure for interval sterilizations using ICD-9-CM procedure codes, and categorized these procedures as laparoscopic or not laparoscopic. Additionally, information on the type of anesthesia (local or general) used in outpatient procedures was available from NSAS.

Women 20-39 years of age were grouped in five-year age intervals, while those aged 40-49 comprised a single group. For the analysis by race, we classified women as white, black, American Indian or Alaska Native, Asian or Pacific Islander, other race or unknown race. Hispanic women were classified by their reported racial group. Due to small sample sizes and large relative standard errors, we do not discuss here any race-specific information on racial groupings other than white and black. Because of the large number of discharges (NHDS) and visits (NSAS) of unknown ("not stated") race (nearly 22% of discharges and 29% of visits), we conducted a sensitivity analysis to evaluate whether apparent differences by race remained statistically significant if all women with unknown race were classified as white (the group with lower rates).

Hospitals and ambulatory surgery centers were classified by location in one of the four geographic regions of the United States, as defined by the U.S. Bureau of the Census: Northeast, Midwest, South and West. Expected primary source of payment was categorized as private insurance (including health maintenance organizations and preferred provider organizations), Medicaid and other.* Region and expected source of payment could not be analyzed by race because of the large percentage with race not stated.

We weighted sampled discharges (NHDS) and visits (NSAS) meeting the case definition to obtain national estimates. To achieve more reliable estimates, we combined the 1994-1996 data; thus, all estimates are based on data for the three-year period. The estimated number of sterilization procedures was based on an unweighted sample of 7,838 hospital records (NHDS) and 5,629 outpatient surgical records (NSAS) for the three-year period.

Rates were calculated as the number of tubal sterilizations per 1,000 women of reproductive age (ages 20-49) in the U.S. civilian resident population. Population estimates for 1994, 1995 and 1996 were computed by the U.S. Bureau of the Census, and are included in the NHDS documentation package. When computing percentage distributions for expected primary payment

source, we excluded discharges (NHDS) and visits (NSAS) with unknown primary payment source (2% of discharges and 4% of visits) from the analysis.

We computed standard errors for estimates derived from the NHDS and NSAS using SUDAAN,⁷ a software package that accounts for complex survey designs. For rates, the denominator was treated as a known quantity (without variance). NHDS and NSAS estimates were considered statistically independent in the computation of standard errors for estimates, which combined data from the two surveys.

Results

We estimate that more than two million women aged 20-49 had a tubal sterilization procedure in the United States between 1994 and 1996. An average of almost 684,000 women underwent tubal sterilization procedures each year (Table 1). The 1994-1996 rate was 11.5 tubal sterilizations per 1,000 women, and the annual rate varied little in the three-year study period.

Approximately half of all sterilizations were performed postpartum and half were interval procedures. All postpartum procedures were performed during inpatient hospital stays, whereas only 4% of interval procedures were performed on an inpatient basis (2% of all sterilization procedures). Most interval sterilizations were performed as outpatient procedures in hospital ambulatory surgery centers or in freestanding surgery centers.

Among women aged 20-29, postpartum sterilization rates were higher than interval rates, whereas the reverse was true among women aged 35-49 (Table 2). Women choosing postpartum tubal sterilization tended to be younger than women electing to have an interval procedure.

Tubal sterilization rates varied by race. Among women whose race was known, postpartum sterilization rates for black women were twice those of white women (Table 3). (For 21% of postpartum procedures, race was not available.) Postpartum rates remained significantly higher among black women than among white women after we recoded to white all cases in which race was not stated. Inpatient and outpatient interval sterilization rates among women with stated race were also higher for black women than for white women; however, the difference was not statistically significant when cases with unknown race were recoded as white.

Sterilization rates were higher in the South than in the other three regions, which had similar rates (Table 4). Regional differences in rates varied by the timing of the sterilization procedure: Postpartum rates were higher in the South than in the other regions, while outpatient interval rates were lower in the West than in any other region.

Overall, private insurance was the expected primary source of payment for the majority of tubal sterilizations nationwide (58%) and in each region (Table 5,

page 164). Medicaid was the expected primary source of payment for one-third of all sterilizations, with this percentage varying from 19% in the Northeast to 37-39% in the West and South. Among women having a postpartum procedure, private insurance was the expected source of payment for 48% overall, while 41% were paid for through Medicaid. In contrast, private insurance was the expected source of payment for the large majority of outpatient interval sterilization procedures (68%), and Medicaid paid for 24%. In the Northeast, Medicaid was the expected source of payment for a smaller proportion of outpatient interval sterilizations than in any other region.

Fifty-eight percent of women who had a postpartum sterilization had a vaginal delivery, and 42% had a cesarean delivery. Among women obtaining an interval sterilization, laparoscopic procedures were used in 89% of outpatient sterilizations and in 53% of inpatient procedures. For women who underwent tubal sterilization on an outpatient basis, general anesthesia was the method of anesthesia used most frequently (in 93% of procedures), while topical or local anesthesia (2%), regional anesthesia (2%) and methods classified as other (6%) were used rarely. (These percentages exceed 100% when totaled because some records indicate more than one type of anesthesia.) Data on anesthesia were not available from NHDS.

Discussion

In the 1970s, tubal sterilization emerged as one of the most common methods of contraception for women of reproductive age in the United States. Female sterilization rates increased from 4.7 per 100,000 women in 1970 to 12.4 per 100,000 by 1980,⁸ and appear to have remained stable over the next two decades, with the rate for 1994-1996 (11.5 per 100,000) being similar to the rate in 1980.

While all postpartum tubal sterilization procedures continue to be performed in hospitals, there has been a significant change in clinical setting for interval procedures in the past 25 years. Technical advances, particularly the use of the laparoscope, have significantly affected the setting in which tubal sterilization procedures can be performed and the trend toward interval sterilization.⁹ In 1970, fewer than 1% of sterilizations not associated with a delivery were performed on an outpatient basis; by 1980, 19% of women having an interval tubal sterilization did not remain in the hospital overnight. Both the number and rate of interval procedures performed in hospitals decreased beginning in 1980, as more ambulatory procedures were performed in hospitals or in freestanding surgery centers. In 1987, 34% of all tubal sterilizations were performed in outpatient settings;¹⁰ this proportion increased to almost 50% by 1994-1996. Although most interval procedures are performed in outpatient settings, a small proportion of interval procedures are performed on an inpatient basis, most likely for medical indications.

The timing of a sterilization procedure influences the surgical approach. Most

inpatient tubal sterilizations are completed by surgical approaches other than laparoscopy. Postpartum sterilizations are performed at the time of cesarean delivery, when the abdomen is open, or following a vaginal delivery, using a 2-5 cm subumbilical minilaparotomy incision.¹¹ Laparoscopy is not used for postpartum sterilization because the size of the uterus would make insertion of the instrument unsafe. Most interval sterilization procedures in the United States are laparoscopic procedures performed under general anesthesia in an outpatient setting. The proportion of interval procedures performed using laparoscopy increased dramatically between 1970 and 1978 (from fewer than 1% to 51%).¹² Laparoscopy continued to increase in usage, from 79% of outpatient interval sterilizations in 1987¹³ to 89% during the current study period.

Similar to what was seen in previous studies,¹⁴ overall tubal sterilization rates in 1994-1996 were highest among women aged 25-34. The peak childbearing years are 20-29,¹⁵ and most women have had the number of children they desire before age 35. As a result of the cumulative effect of sterilizations over the reproductive age span, 50% of all contraceptive users 40-44 years of age relied on female sterilization in 1995.¹⁶

Tubal sterilization rates among black women were more than twice those of white women in 1970 (9.0 versus 4.1 per 100,000).¹⁷ Although by 1975 tubal sterilization rates had increased twofold among white women and differences by race had narrowed,¹⁸ rates increased more for black women and have remained higher than those for white women since 1976.¹⁹ Our ability to conduct analyses by race in this article was limited because of the high proportion of procedures with unknown race (21-29%), and because hospitalizations in the NHDS for which the patient's race is marked as unknown are not proportionally distributed among all race groups.²⁰ Comparisons of data from the NHDS with data from other sources suggest that race was underreported to a greater extent for white patients than for patients of other races.

While our results must be interpreted with caution, the differences we found between black and white postpartum rates are large enough to remain significant when all women whose race was not stated are added to the white category. This difference by race in some sterilization rates may be explained in part by the fact that non-Hispanic white married or cohabitating women rely on vasectomy as a method of permanent sterilization more frequently (10%) than do black married or cohabitating women (1%).²¹ Women who choose tubal sterilization tend to be less-educated and to have lower levels of income,²² likewise, black women have been shown to have lower levels of income, education and access to health care.²³ These and other factors, rather than race itself, most likely account for differences between black and white women in tubal sterilization rates.

We found that regional differences in overall tubal sterilization rates continued in a pattern similar to those reported for the 1970s and 1980s, with the South having the highest rates.²⁴ Notable in our findings are the higher share of interval versus postpartum procedures in the Northeast and Midwest, compared with an inverse relationship between interval and postpartum rates in the South and West. Although our data do not provide insights into the reasons for regional differences, other researchers have suggested that these may be due in part to variations in physicians' attitudes toward sterilization, in the medical care delivery system and in patients' religious beliefs.²⁵ Offsetting variations in vasectomy rates may also account for regional variations in tubal sterilization rates, although published studies have presented conflicting estimates of regional vasectomy rates.²⁶

Previous studies have not examined the source of payment for tubal sterilizations. We found significant differences by region and timing of procedure in the expected primary source of payment. In all regions, Medicaid was the expected source of payment for a higher proportion of postpartum tubal sterilizations than of outpatient interval sterilizations. This difference is explained by Medicaid restrictions in most states limiting coverage of family planning services, including tubal sterilization, for Medicaid recipients to 60 days postpartum.²⁷ Although nine states had expanded coverage under their Medicaid programs by 1997 to include eligibility for family planning services, in most of these states the expanded coverage was restricted to no more than two years' postpartum for Medicaid recipients or up to two years after loss of regular Medicaid coverage.²⁸ In contrast, women covered by private insurance have greater latitude in choosing the timing of their sterilization, given that tubal sterilization is routinely covered by 85-90% of private health insurance policies.²⁹ In addition, the 30-day waiting period required for federally funded sterilization may adversely affect women covered by Medicaid, compared with women who have private insurance; we cannot measure that impact in this study, however.

Several limitations of this study need to be considered. The estimates of sterilization reported here are lower than the total number of tubal sterilizations in the United States, because our analysis did not include any tubal sterilizations performed in federally operated hospitals and clinics or in family planning clinics. However, in 1987, the Association for Voluntary Surgical Contraception reported that only 2% of all sterilizations were performed in military hospitals and family planning clinics.³⁰

Another shortcoming is that our calculation of tubal sterilization rates includes already-sterile women in the denominator; if women who were already sterile from previous tubal sterilization, from hysterectomy or as a result of other medical conditions were excluded from the denominator, tubal sterilization rates would be higher. Further, the apparent decline in sterilization rates with

increasing age would be less dramatic if rates were based only on women at risk.

Additionally, differences in methodology used to determine outpatient estimates preclude a strict comparison with some previous reports.³¹ Finally, race and ethnicity are not available for all records (as previously discussed), and rates for specific race groups are underestimated to an unknown extent.

A number of factors may affect future trends in sterilization. Recent shifts toward delayed childbearing³² may reduce the number of younger women choosing tubal sterilization. Women marry later and wait longer after marriage to start families.³³ In addition, although early reports suggested an increased risk for cardiovascular disease among oral contraceptive users of older ages, data now support pill use among healthy women older than 35 who do not smoke.³⁴ While overall use of oral contraceptives declined between 1988 and 1995, pill use doubled among women aged 35-39 and rose sixfold among those aged 40-44.³⁵ These factors may increase the age at which a woman considers permanent contraception and the rates at which they choose sterilization.

This study is the first comprehensive analysis of all tubal sterilizations since 1987. Our report updates trends in timing, setting and surgical method of sterilization procedures, and provides information on differences by region and source of payment. The availability of NSAS data from outpatient surgical facilities during 1994-1996 has provided key information for a more complete analysis of tubal sterilization rates in the United States.

While NHDS and NSAS offer the most comprehensive data on tubal sterilizations for 1994-1996, further research would be enhanced by data on patient characteristics not available from these surveys, such as parity, prior method of contraception, marital status and education. In addition, improved reporting of race would allow for an analysis of the interaction of race, region and source of payment.

Currently, national data are not collected annually on procedures performed in hospital ambulatory surgery centers or freestanding surgery centers; NSAS was only conducted during the 1994-1996 time period. Clearly, data on inpatient sterilizations from NHDS, used to determine sterilization estimates in the 1970s and early 1980s, are no longer representative of all sterilizations. Continued surveillance of both inpatient and outpatient procedures is needed to monitor the role of tubal sterilization in contraceptive practice.

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*The "other" category included self-pay, Medicare, other government payments and those marked as "other, specified."

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Deaths attributable to tubal sterilization in the United States, 1977 to 1981

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In 1979, the Centers for Disease Control began surveillance of deaths attributable to tubal sterilization in order to determine why they occur and what may be done to prevent them. Since that time, 29 such deaths have been identified as occurring in the United States from 1977 through 1981. Of these 29 deaths, 11 followed complications of general anesthesia, seven were due to sepsis, four were due to hemorrhage, three were due to myocardial infarction, and four deaths were related to other causes. Some of these deaths might have been prevented by use of endotracheal intubation for general anesthesia, particularly for laparoscopic sterilization, safer use of unipolar coagulation or use of alternative techniques, careful insertion of the needle and trocar for laparoscopy, and discontinuation of oral contraceptives before sterilization. Further surveillance may help to make tubal sterilization even safer. (AM. J. OBSTET. GYNECOL. 146:131, 1983.)

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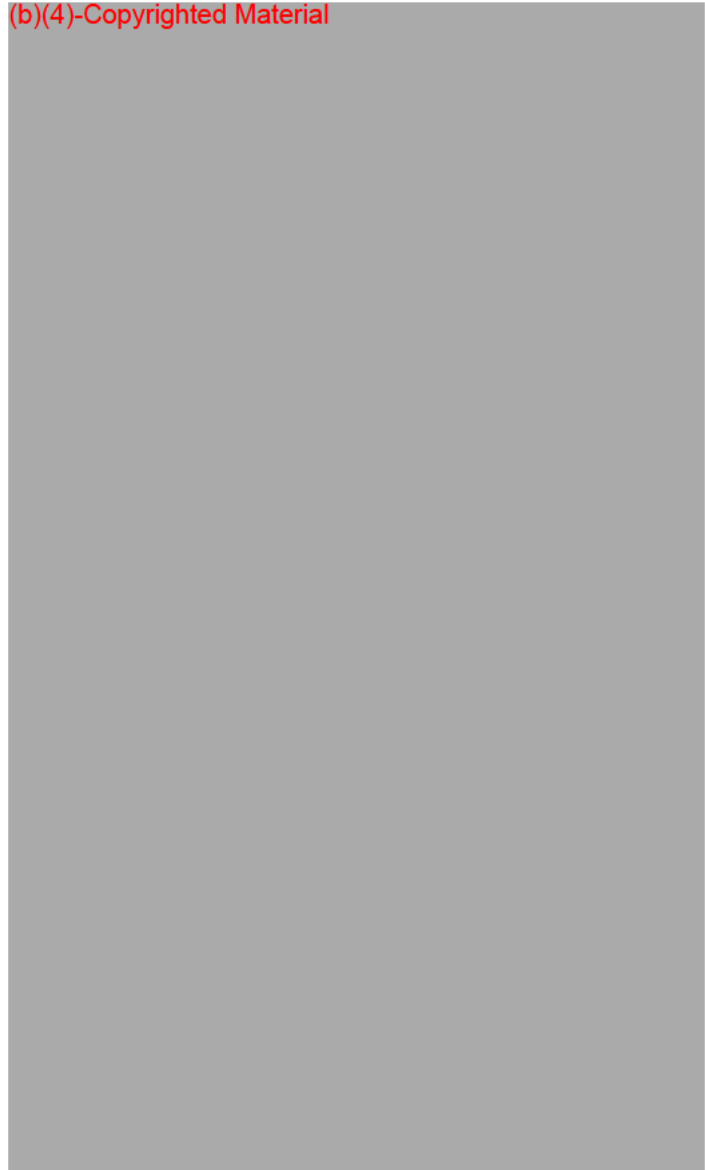
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Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study

HERBERT B. PETERSON, MD, JAROSLAV F. HULKA, MD, FRED J. SPIELMAN, MD, SARA LEE, BS, AND POLLY A. MARCHBANKS, PhD

Despite the contention by some that local anesthesia is a preferred alternative to general anesthesia for laparoscopic sterilization, there have been no randomized studies comparing these techniques. To better characterize the relative safety and acceptability of these techniques for laparoscopic sterilization, we randomly assigned 100 women undergoing bipolar electrocoagulation or spring clip application to either local or general anesthesia. Of the 53 women assigned local anesthesia, four had their procedures completed using another technique because of technical problems related to obesity. Thirteen other obese women, however, underwent successful surgery with local anesthesia. Women undergoing local anesthesia had a slightly shorter anesthesia time (30 versus 36 minutes) and recovery room stay (65 versus 78 minutes). Women having general anesthesia were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate 110 or higher. Patient movement was reported to be a concern in five women undergoing general anesthesia, but in none having local anesthesia. An equal percentage (80%) of women in each group expressed satisfaction with their anesthetic technique. (*Obstet Gynecol* 70:903, 1987)

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The risk of pregnancy after tubal sterilization: Findings from the U.S. Collaborative Review of Sterilization

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OBJECTIVE: Our purpose was to determine the risk of pregnancy after tubal sterilization for common methods of tubal occlusion.

STUDY DESIGN: A multicenter, prospective cohort study was conducted in U.S. medical centers. A total of 10,685 women who underwent tubal sterilization was followed up for 8 to 14 years. The risk of pregnancy was assessed by cumulative life-table probabilities and proportional hazards models.

RESULTS: A total of 143 sterilization failures was identified. Cumulative 10-year probabilities of pregnancy were highest after clip sterilization (36.5/1000 procedures) and lowest after unipolar coagulation (7.5/1000) and postpartum partial salpingectomy (7.5/1000). The cumulative risk of pregnancy was highest among women sterilized at a young age with bipolar coagulation (54.3/1000) and clip application (52.1/1000).

CONCLUSIONS: Although tubal sterilization is highly effective, the risk of sterilization failure is higher than generally reported. The risk persists for years after the procedure and varies by method of tubal occlusion and age. (Am J Obstet Gynecol 1996;174:1161-70.)

Key words: Tubal sterilization, pregnancy, sterilization failure

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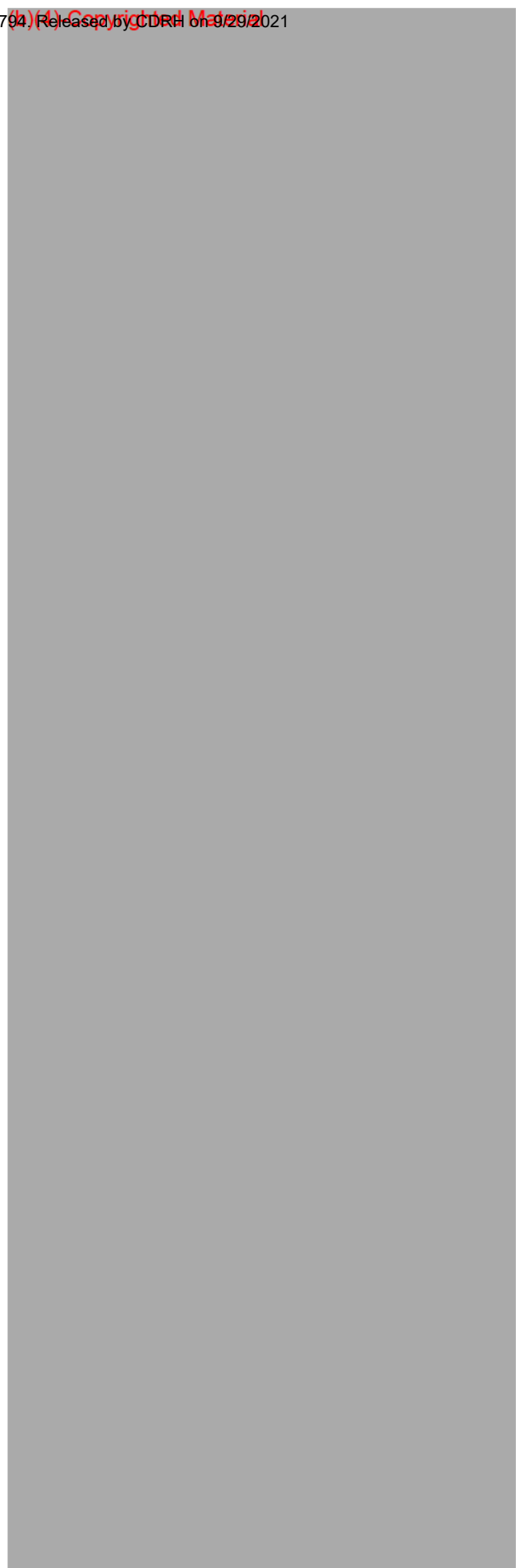
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Contraceptive Method Choice in Developing Countries

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CONTEXT: For all persons to enjoy a choice among contraceptive options, a range of methods must be readily available. Yet measures of access show serious deficits that depress use of each method. Countries differ both in the number of methods offered and the extent to which each is made available. Information is needed on how these factors have changed over time and how they have affected contraceptive use overall and use of individual methods.

METHODS: Patterns of contraceptive use are derived from data from national surveys, and levels of access to four methods (female sterilization, the IUD, the pill and the condom) are measured by estimates from cycles of a program effort study of the proportion of couples for whom each method is available, as of 1982, 1989, 1994 and 1999. The analysis focuses on the relationship between access to contraceptives and patterns of use.

RESULTS: In all four cycles of the program effort study, the mean prevalence of the four methods rises with mean access. For example, mean prevalence in 1994 and 1999 was close to 12% in countries with very low access, compared with 44% in those with high access. Prevalence is highest in countries where access to all methods is uniformly high. In 1994, for example, mean prevalence was 12% in countries where mean availability was high and diversity in the availability of individual methods was low, compared with 9% in countries where mean availability was high and access to individual methods varied considerably. Between 1982 and 1994, the number of countries with uniformly high access rose from nine to 23, while the number with uniformly low access declined from 23 to nine. At the lowest level of mean availability, the condom and the pill contribute most to availability (40% and 36%, respectively), but at the highest level, the contributions of the four methods equalize at 22–27% each. The situation for prevalence is similar: The pill's share at the lowest level of availability is 67%, compared with 31% at the highest level, where it is surpassed by female sterilization (36%).

CONCLUSIONS: Full choice among a variety of contraceptive offerings is yet to be attained in many countries. Its absence restricts personal access to each method as well as the use of all methods in the population. To the extent that the ability to choose satisfactory contraceptive protection depends on ready access to multiple methods, a clear mandate exists for greater programmatic attention to the provision of a full range of methods.

International Family Planning Perspectives, 2001, 28(1):32–40

The report of the International Conference on Population and Development issued the following directive:

"Recognize that appropriate methods for couples and individuals vary according to their age, parity, family size-preference and other factors, and ensure that women and men have information and access to the widest possible range of safe and effective family planning methods in order to enable them to exercise free and informed choice."¹

The reality in most countries, however, is far different. Most countries offer only a limited choice of contraceptive methods, and couples cannot easily choose the method that best suits their reproductive needs.² In fact, international program effort scores for 1994 showed that large proportions of people in most developing countries did not have ready access to a variety of contraceptive methods.³ Couples had essentially no access to the IUD in 30 countries, no access to female sterilization in 37 and no access to vasectomy in 61. Many African countries had low access scores on almost every method. Five years later, in the 1999 rat-

ings for 88 countries, only 65% of countries offered the pill to at least half their population, 54% the IUD, 42% female sterilization, 26% male sterilization and 73% the condom.⁴

Substantial evidence indicates that a restricted choice of contraceptive methods has constrained the opportunity of individual couples to obtain a method that suits their needs, resulting in lower levels of contraceptive prevalence. One study noted that in Taiwan, each new method seemed to add another layer of use to existing prevalence; similar increases were evident in South Korea, Thailand and Hong Kong.⁵ A second study found that broadening the choice of contraceptive methods increased overall contraceptive prevalence in Matlab, Bangladesh, where household provision of injectables in early 1977 helped raise contraceptive prevalence from 7% to 20%, the introduction of tubectomy services in 1978 helped increase prevalence by an additional 10 percentage points, and household insertion of IUDs in 1981 elevated prevalence yet further.⁶ Jain has estimated that the widespread addition of one method to

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the options available in a country would be associated with an increase of 12 percentage points in contraceptive prevalence.⁷ Behind these figures lie increased numbers of satisfied couples, as well as fewer unplanned pregnancies, induced abortions and unwanted births.

This article is devoted to the issue of choice, which in part depends on the widespread availability of a variety of contraceptive methods. We examine the overall level of use and the diversity of use of contraceptive methods in relation to their measured availability. Although it is beyond the scope of this article to deal with important issues of client treatment, policymakers and planners should consider them along with the issues of method availability addressed here.

DATA AND METHODOLOGY

Availability of Contraceptive Methods

This article uses the ratings of method availability obtained in studies of national family planning programs conducted in 1982, 1989, 1994 and 1999.⁸ In each cycle, 30 features of program effort were measured, including some that focused specifically on the availability of contraceptive methods to the general population. Four modern methods that are provided through large-scale programs—the condom, the pill, the IUD and female sterilization—are included here. Others, such as the implant, the injectable and male sterilization, are omitted either because separate estimates are unavailable in the effort ratings or because, like the implant and male sterilization, the methods exhibit very low levels of use and availability.*

Contraceptive Use

Data on contraceptive use are taken from national surveys, including the World Fertility Surveys (WFS), Contraceptive Prevalence Surveys (CPS) and Demographic and Health Surveys (DHS). The key indicator is the percentage of couples using each method at the time of the survey, based on responses by married or cohabiting women of reproductive age (usually those aged 15–49). Having data from multiple surveys over time for a given country allows us to estimate contraceptive use, by method, at approximately the same dates as the effort scores, by interpolating between survey dates or, in some cases, by extrapolating from historical trends. The prevalence information relates to use for family planning purposes; thus, condom use for protection against sexually transmitted diseases is very likely underestimated.

Availability Measures

Sixty-four countries had information on program effort scores for all three years (1982, 1989 and 1994), and also had survey estimates for contraceptive prevalence. (These 64 countries are home to 91% of all women aged 15–49 who live in the 110 developing countries with populations of more than one million each. Only 47 countries had both program effort estimates and recent survey estimates for 1999; for certain analyses, we combine the 1994 and 1999 scores and use the total of 64 units of observation.

Method availability is measured through the program effort scores as the percentage of the population having ready and easy access to each contraceptive method.¹ The percentage for each method comes from respondents' estimates for the urban and rural sectors, which we combined with population weights to obtain the national figure.

Method availability is distinct from method use: The condom, for example, may be easily available but little used; in fact, its level of use for family planning has usually been quite low. The proportion of women relying on sterilization, on the other hand, can rise to a substantial figure over time, although its availability at any one time may be modest. Respondents to the program effort questionnaire were cautioned not to confuse availability with actual use, but to estimate the percentage of the population having access without reference to the percentage that might be using it.

Analytic Approach

In the following sections, we examine the association between method access and prevalence by first summarizing improvements in availability and prevalence over time, by region; by using all methods to relate mean prevalence to mean availability; by relating availability and prevalence for each method alone; by relating prevalence simultaneously to both the level and the diversity of method availability; and by documenting the relative contribution of each method to both availability and prevalence over time, subject to the overall availability level.

RESULTS

Access and Prevalence Improvements

Over the period 1982–1999, the average availability score for the group of four methods included here rose from 1.5 to 2.6, the equivalent of access for 30–52% of the population. The availability of each individual method also rose substantially, from 25% to 35% for female sterilization, from 34% to 61% for the pill, from 26% to 50% for the IUD and from 34% to 63% for the condom.

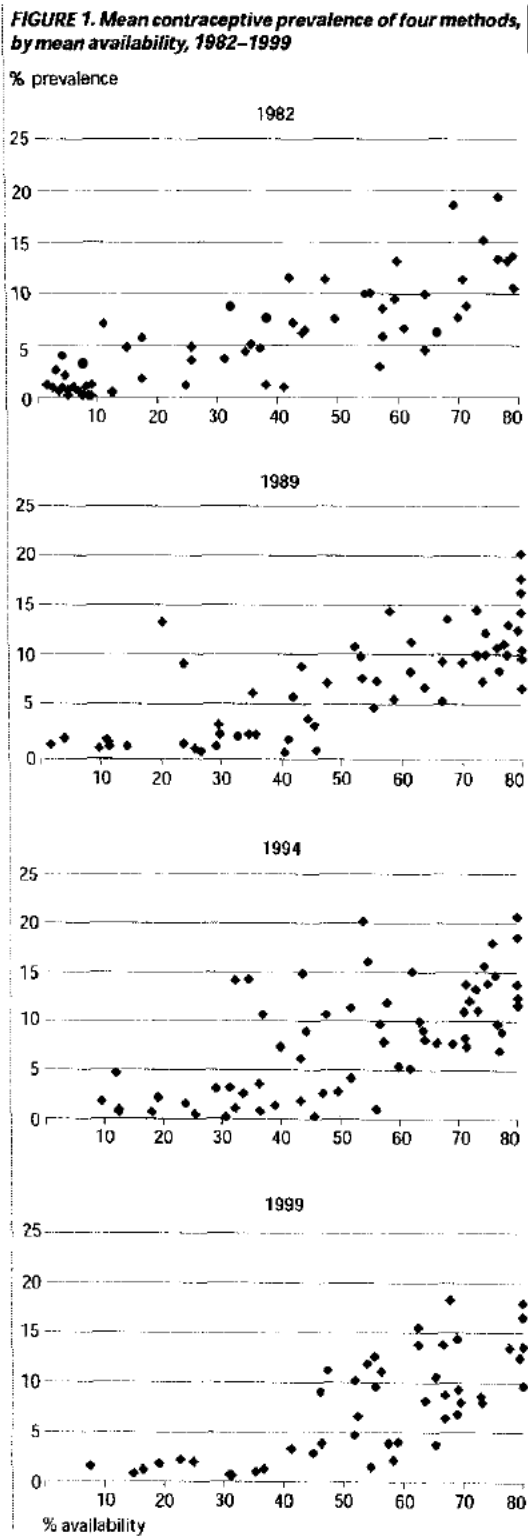
Regional differences are considerable, with availability greatest in East Asia and least in Sub-Saharan Africa—especially the francophone countries. The other regions are clustered in a middle range. East Asia attained a high level of availability early in the study period and experienced little change thereafter; on the other hand, Sub-Saharan Africa shows recent improvements, although at fairly low levels. Condom availability seems to have increased more sharply in Africa and Asia than in Latin America, while the availability of female sterilization appears to have risen most in Latin America.

Like availability, the prevalence of contraceptive use has risen markedly over the decades. The latest United Nations

*Including these methods would tend to strengthen the association between limited choice and low prevalence, but it is already evident that the literal absence of methods means nonuse, and the presence of many near-zero values would obscure the correlations for the more common methods.

¹Respondents were instructed that "ready and easy access" means spending no more than an average of two hours per month to obtain the service or supply and that the cost of one month's supply of the service or supply should be less than 1% of a month's wages.

Contraceptive Method Choice in Developing Countries



review, using surveys that cover 85% of the developing world's population, shows that "almost all of the less developed countries with trend data experienced an increase in the level of contraceptive use."⁹ Over an average period of 9.5 years, use increased by at least one percentage point

per year, or 10 points per decade, in more than two-thirds of the countries and by two points or more annually in 11% of the countries. By region, the UN's medium estimate is highest for East Asia (83% of couples using a method), followed by Latin America and the Caribbean (66%), other Asian regions (44%), northern Africa (42%) and Sub-Saharan Africa (14%).

Mean Availability and Mean Prevalence

In all four cycles of the program effort study (1982-1999), mean prevalence and mean availability are closely and positively related (Figure 1). The relationship persists as countries improve in both variables over the four years—that is, as they shift upward and to the right. This finding is consistent with the hypothesis that better choice, via easier access to methods, leads to use by more couples, which may imply greater satisfaction and fewer unwanted pregnancies.

The 64 countries in the study are shown in Figure 2, which classifies them jointly by average availability and prevalence. The overall prevalence in the 64 countries was 32%, rising from 6% in the very low prevalence countries to 59% in the high-prevalence nations. (These figures are for only the four modern methods included in the study, so they are lower than totals for all methods, including traditional methods.) Mean prevalence increased with access; it was only 12% in countries with very low access, compared with 44% in countries with high access.

The data for 47 countries pertain to 1999 and those for 17 countries pertain to 1994; because patterns in 1994 and 1999 were similar, we used all 64 units of observation. We divided the 64 countries into four availability groupings of equal size, as well as four prevalence groupings of equal size; the two sets of groups were then cross-classified. This procedure places 16 countries in each row and in each column; if there were no association between availability and prevalence, the countries would be evenly distributed across the cells.

In fact, most countries cluster along the diagonal in the table, from very low values to high values on both characteristics. Fifty-three of the 64 countries either lie in cells directly on the diagonal or in adjoining ones; only 11 are in cells that are further away. Not unexpectedly, most countries in the upper-left cell (i.e., those with very low prevalence and very low availability) are in Sub-Saharan Africa, whereas most of the countries in the lower-right cells (those with high prevalence and high availability) are in Latin America and Asia. When the original values for average availability and prevalence are used, the correlation is 0.41. For each country, the average prevalence for the four modern methods in the study appears in the cells. As one would expect, it is lower than published figures for all methods (including traditional methods).¹⁰

One question is whether the respondents who rated the availability of each method might have been influenced by their impressions of prevalence levels; if so, the assumption of independent measurements might be compromised and the correlation between availability and prevalence

FIGURE 2. Prevalence of use of four modern contraceptive methods (the pill, condom, IUD and female sterilization), by mean overall level of method availability and overall level of prevalence, 64 countries, 1994 or 1999

Mean availability	Mean prevalence								Mean prevalence (N=64)
	Very low (N=16)		Low (N=16)		Medium (N=16)		High (N=16)		
	Country	%	Country	%	Country	%	Country	%	
All		6.2		22.4		39.5		58.6	31.7
Very low	Mean	5.6	Mean	18.8	Mean	46.0	Mean	0.0	11.5
	Benin	2.4	Iraq*	18.8	Panama*	46.0			
	Ethiopia	2.8			Guyana*	46.0			
	Niger	3.2							
	Nigeria*	3.6							
	Mali	4.0							
	Madagascar	4.8							
	Uganda	5.2							
	Mauritania*	5.6							
	Cameroon	6.4							
	Sudan	7.2							
	Malawi	8.0							
	Tanzania	8.8							
	Lesotho*	10.4							
Low	Mean	8.8	Mean	18.9	Mean	40.8	Mean	59.6	32.2
	Haiti	11.6	Syria*	23.6	Jordan	36.4	Egypt	47.6	
	Senegal	6.0	Zambia	13.2	El Salvador	44.8	Cuba*	80.8	
			Nepal	15.6	Zimbabwe	40.8	Jamaica	50.4	
			Kenya	18.8	Honduras	38.4			
			Guatemala	26.4	Ecuador	44.4			
			Pakistan	15.6					
Medium	Mean	8.8	Mean	20.8	Mean	37.2	Mean	58.4	39.5
	Ghana	8.8	Bolivia	16.0	Iran*	39.2	Kuwait*	48.4	
			Oman	15.2	India	32.8	Costa Rica	62.0	
			Philippines	25.6	Morocco	42.4	Vietnam	55.2	
			Indonesia	27.2	Turkey	35.2	Rep. of Korea	55.2	
					Sri Lanka	37.2	China	73.2	
							Dom. Rep.	57.6	
High	Mean	0.0	Mean	28.4	Mean	37.2	Mean	58.1	43.6
			Peru	32.0	Mauritius*	35.2	Colombia	54.0	
			Malaysia*	24.0	Paraguay	34.4	Thailand	50.0	
			Bangladesh	32.0	Algeria	38.8	Brazil	66.4	
			Trinidad & Tobago*	31.2	Venezuela*	40.0	Mexico	54.4	
			Botswana*	22.8			Singapore*	62.8	
							Taiwan	72.0	
							Tunisia*	46.8	

*Data are for 1994.

might be affected. However, explicit instructions are given in the program effort questionnaire that access measures are not the same as actual use and that the two are not to be confused. The respondent is asked to estimate the percentage of the population with access to each method, without regard to the level of use. Each method is listed individually, with separate entries for the rural and urban sectors.

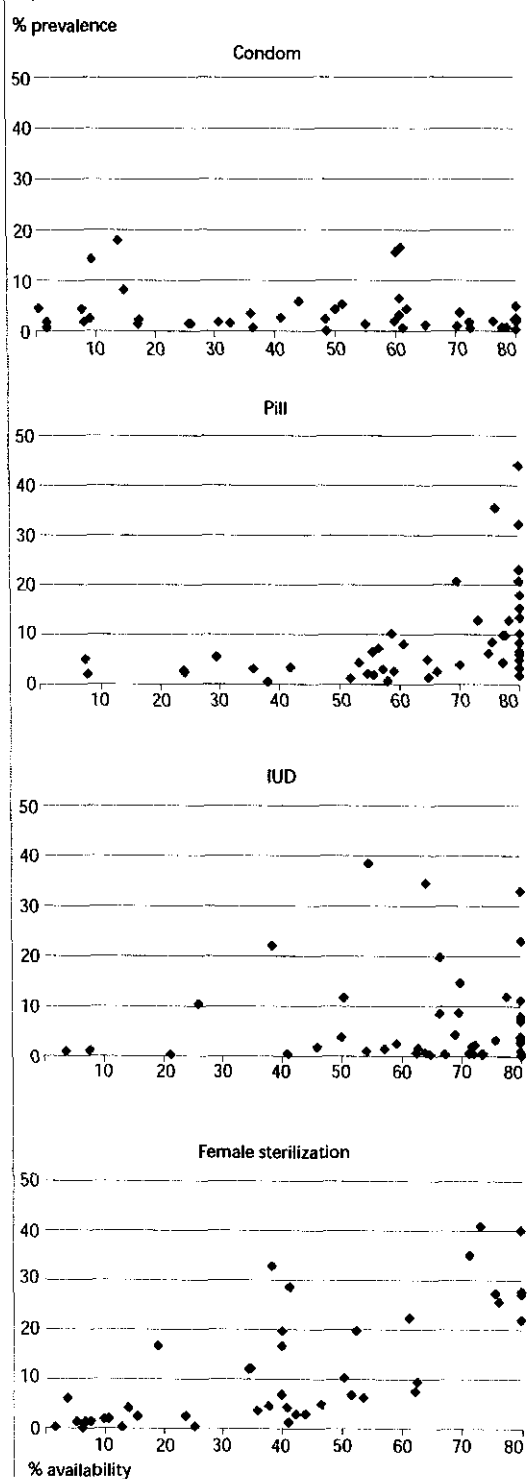
One check on the accuracy of the availability information is afforded by DHS survey information on the percentage of women who know of a source for a given method. That measure is a more objective indicator, and knowledge of a source for a particular method should correspond generally to the actual availability of the method. Some DHS country reports do not include source information, but it is available from data tapes for 20 country surveys conducted between 1990 and 1993.¹¹ Correlations for 1994 between availability and knowledge of a source for the four

methods are highly significant, at 0.39 for female sterilization and the pill and 0.47 for the IUD but only 0.10 for the condom. Each correlation is higher when the 1989 availability data are used (0.43, 0.46, 0.65 and 0.17). These patterns, in both years, give partial support to the usefulness of the availability ratings. Results from one study cycle to the next have shown a consistency in the associations, even as the levels of program effort have risen.¹²

The correlations in question necessarily reflect reality to some extent, because use cannot exist without access. The use level sets a minimum level for what access must be; moreover, access to a contraceptive method always exceeds its use, because many couples who could use the method prefer, and use, other methods. The true degree of association between access and use is as likely to be obscured as heightened by any nonindependence between the measures. The data for different countries are reported by different respondents, who would vary in the access rating they

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FIGURE 3. Contraceptive prevalence, by availability, according to method, 47 countries, 1999



would give for any known level of use, with variations in the gap between use and access. This process would add confusion to the data, attenuating the true association; further, any influence of partially outdated survey materials would obscure the association rather than inflate it. The

assumption throughout is one of an independent estimate of access, quite apart from the level of use, and any weakening of this assumption is thought to be small in comparison with the overriding dependence of use on access.

Availability and Prevalence of Methods

Except for the condom, the use of each method is highest where the availability of that method is high. For example, in the countries with greatest use of the pill (36–44%), the level of availability is 76–80%. Likewise, the highest prevalence of female sterilization (35–41%) is found in countries where 71–80% of the population have access to the method.

The patterns shown in Figure 3 reflect a crowding of some countries at the maximum value, which as noted is 80–100% of the population. Figure 3 is restricted to 1999; in earlier years, the patterns were similar, but countries were clustered at lower values of both availability and prevalence.* Except for the results for the condom, this method-specific examination of availability and prevalence supports the results shown in Figure 1 for the means of availability and prevalence of the four methods together.

Prevalence Related to Availability

When the mean level of availability is in the middle range, the diversity (variation) among methods can be either great or small. That is, the same mean can result from all four methods being equally available or from variation among them—e.g., with two at high levels and two at low levels. In the first case, some of the population has basic access to all four methods; in the second case, the population has more access to two methods, but less to two others. Also, depending on how the various methods are geographically distributed, access to individual methods may vary across subgroups, as when urban residents live near facilities that offer the IUD and sterilization and rural residents are served by programs that distribute the pill and the condom.

Here we explore how prevalence relates to the interplay of the level and diversity of availability, with diversity measured by the standard deviation across the four methods. We begin by comparing countries that have a low mean for the availability of all four contraceptive methods with countries that have a high mean. The preferred situation is relatively high mean availability and a low standard deviation, meaning that all methods are easily and uniformly accessible. The reverse case is the unfortunate combination of a low mean and a low standard deviation, indicating that all methods are uniformly unavailable. Contraceptive prevalence is expected to be quite high in the first instance and quite low in the second. (Note that a very high or a very low mean can occur only with a very low standard deviation, because diversity among methods precludes extreme averages.)

For couples to enjoy a good choice, they need ready access to a variety of methods; in that case, each method will

*Female sterilization is different, in the sense that a country can attain high prevalence over the years even though availability is modest in each year. A low annual adoption rate still tends to produce high prevalence in the long run because continuation is so prolonged.

TABLE 1. Mean contraceptive prevalence in 64 countries, by mean availability and year, according to standard deviation of availability

Mean availability and year	Standard deviation			
	High		Low	
	Mean prev.	No. of countries	Mean prev.	No. of countries
High				
1982	8.3	23	10.9	9
1989	9.3	10	11.5	22
1994	9.1	9	11.8	23
Low				
1982	4.0	9	1.9	23
1989	4.1	22	2.3	10
1994	6.2	23	3.6	9

Note: Data pertain to only four methods—female sterilization, the IUD, the pill and the condom.

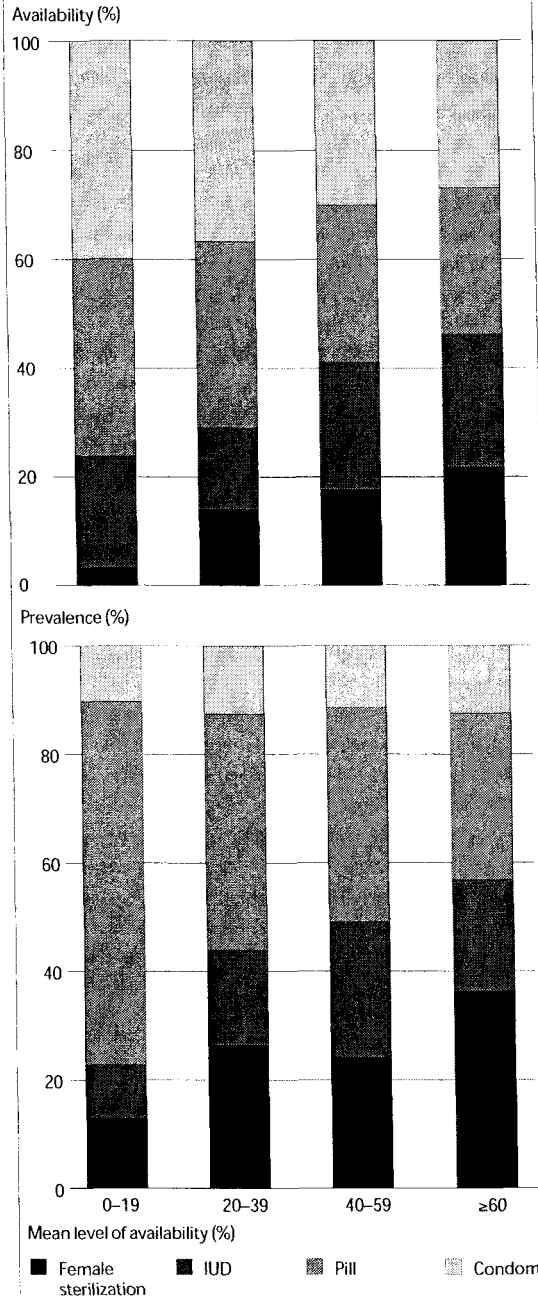
find its own subgroup of users in the population. That situation should in turn lead to substantial prevalence values for each method, and therefore a high total, because most couples would be able to choose a method that fits their stage of life and their reproductive health status and reflects their experience with other methods.

To test this concept, we constructed a two-by-two table in which mean contraceptive availability in a country is classified as either low or high, and the standard deviation is also classified as low or high (Table 1). We used data for 1982, 1989 and 1994 because the greater number of countries (64) provides more stability than the number for 1999 (47). For each year, the 64 countries are divided evenly above and below the median for availability; the procedure is repeated using the median for the standard deviation, so that the numbers of observations for analysis are balanced. This places 32 countries in each row, by year, and 32 countries in each column, by year. We expect that prevalence will be highest where mean availability is high and the standard deviation is low (upper-right quadrant) and that prevalence will be lowest where both the mean and the standard deviation are low (lower-right quadrant). In fact, prevalence values correspond to these expectations in all three years. In addition, as expected, the prevalence values rise over time.

The table also reveals trends over time in levels of and diversity in availability. In the top half of Table 1, the distribution of countries shifts: In 1982, 23 of the 32 countries with high mean availability had a high standard deviation, but by 1989, 22 had a low standard deviation. This trend implies that availability became more uniform across methods as access to the less readily obtained methods rose to match the already high level of access to the others. Also, the favorable upper-right quadrant gained members between 1982 and 1989, while the unfavorable lower-right quadrant lost members, reflecting a movement toward uniformly high access, a pattern that held in 1994.

Table 1 isolates the various combinations of high and low values, but the limited sample size makes it necessary to use broad categories. Multiple regression analyses indicate that

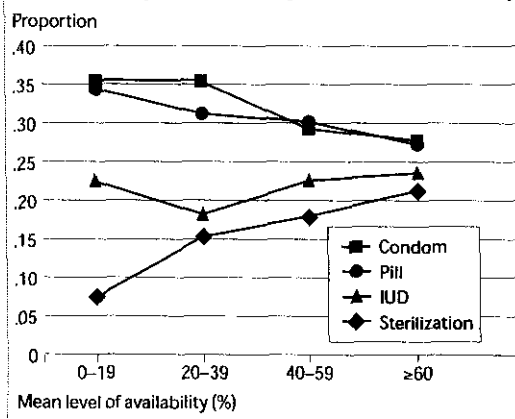
FIGURE 4. Percentage distribution of contraceptive availability and prevalence, by method, according to mean level of availability, 1994



total availability is a more important determinant of prevalence than the standard deviation; however, high total availability automatically incorporates a low standard deviation because values for all methods must be uniformly high.*

*In addition, the role of the standard deviation is masked by the assumption of linearity in the regressions. The standard deviation is low at both high and low values of the mean, and the interaction is an important element. The standard deviation is large only at intermediate values of the mean. Scattergrams confirm a marked U-shaped (upside down) relation between the mean and the standard deviation for each of the four contraceptive methods.

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FIGURE 5. Proportion of total contraceptive prevalence accounted for by each method, by mean level of availability

Note: Values shown are averages of 1982, 1989 and 1994 data.

In summary, Table 1 captures the essence of the situation, that the special combination of high availability and low standard deviation best predicts high prevalence of use. Likewise, personal choice is maximized in an environment that gives uniformly high access to several contraceptive methods.

Contribution of Individual Methods

• **Availability.** To analyze the relative contribution of the various methods to the availability score, we divided the 1994 data set with 64 countries into four access groupings: Level 1 (those where mean availability is less than 20%), Level 2 (those where it is 20–39%), Level 3 (where it is 40–59%) and Level 4 (where it is 60% or greater). The contribution of each method is simply its share of the total—that is, each method's access taken as a percentage of the total access for all methods (Figure 4, page 37).

For Level 1 countries, the pill and the condom—both supply methods—contribute most to the mean availability score (36% and 40% of the total, respectively). The IUD and female sterilization together contribute only about 24% to the score. At Level 2, the relative contributions of the pill and the condom parallel those seen at Level 1, while the contribution of the IUD decreases and that of female sterilization increases (from 3% to 14% of the total). At Level 3, the contributions of female sterilization and the IUD both increase. Finally, at Level 4, the four methods reach a fairly even balance, at 22–27% for each. This balance reflects an improved set of choices for couples in countries at Level 4, and it shows the dependence of total availability on the presence of multiple methods.

• **Prevalence.** Figure 4 also shows the contribution of each method to total prevalence at each availability level. It is interesting to compare the two patterns: The contributions of each method to availability and prevalence agree more closely as mean availability increases. The pill contributes

*The prevalence of every method can increase in the general population even during a shift in the shares of use. The changing shares reflect only the relative growth rates among the methods.

disproportionately to prevalence at the lowest level of availability (67% of the total), and loses share with each increase in level. The condom's contribution remains about the same, so the contribution of the two resupply methods combined diminishes proportionately as overall availability rises across levels. The relative contributions of the IUD and sterilization increase, so at the highest level of access, sterilization accounts for 36% of users, the pill 31%, the IUD 21% and the condom 12%. *

Although Figure 4 is concerned with proportionate contributions of the four methods, the absolute values for availability far exceed those for prevalence of use. At every level of mean availability, the proportion of the population with access to a given method is greater than the proportion using it. That is a necessary result; if each of the four methods were available to half of the population, total use could still be only about 85% of all couples, an approximate ceiling level in high-prevalence countries. Levels of use may also be depressed below availability levels because of a variety of barriers that interfere with the adoption of contraceptives.

Finally, we merged data for three years—1982, 1989 and 1994—to study the movement toward an even method mix as overall access improves (Figure 5). In countries with poor overall availability (on the left hand side of the figure), the pill and the condom dominate; in countries with better access (on the right), the methods have similar shares centered on 25%. Total prevalence is higher in such countries, as couples with differing needs are able to find a satisfactory method and continue its use.

DISCUSSION AND RECOMMENDATIONS

The freedom to choose from a range of contraceptive methods, according to one's needs and preferences, rests partly on the sheer availability of those methods. While it is certainly true that family opposition, fear, cost and uncongenial supply sources also affect choice, our data show that the availability of methods and the prevalence of their use are intimately related. In general, the prevalence of use of each method follows its availability, the mean prevalence of all methods follows mean availability and total prevalence follows the availability of several methods that are each easily available.

Intermediate mean levels of availability and prevalence sometimes hide imbalances in the method mix. The same mean can reflect either unevenness or uniformity, with only two methods dominating (as in China) or with a mix of several methods (as in Thailand). The very highest means, however, require uniformly high levels of availability for every method involved, the optimum situation for full freedom of choice for individual couples.

An examination of availability data over time suggests an historical trend in program development that countries usually do not improve access to all methods at the same time. Rather, they tend to improve access to one or two methods and only later attend to the others: At low average levels of availability, supply methods (pills and condoms) are most readily available; as the average level of availability

rises, access to the IUD and female sterilization increases. While concentrating on one or two methods may be simpler administratively at the start and provide couples with early access to at least something, it also restricts full choice in the middle phase of program development.

The large difference between method availability and use in low-prevalence countries indicates that other factors act as brakes on use. This suggests a continuing need to examine nonaccess barriers, encompassing the whole range of implicit and explicit policies. These obstacles¹³ include excessive medical barriers, unneeded eligibility criteria, poor public information, and lack of training or biases among program staff regarding certain methods. In some cases, an entrenched program subculture limits clients' choices to only one or two favored methods, leaving unserved the persons for whom these methods do not work. Clearly, public policy needs to address not only the variety of contraceptive methods that are present in the environment, but also the many barriers that impede their use.

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RESUMEN

Contexto: Para que todas las personas puedan disfrutar del uso del anticonceptivo de su elección, se debe tener a disposición una amplia gama de métodos. Todavía las medidas de acceso presentan serias limitaciones que limitan el uso de cada método. Los países difieren tanto con respecto al número de métodos que se ofrecen como la disponibilidad de cada uno. Se necesita información acerca de la forma en que estos factores han cambiado a través del tiempo y sobre la manera en que han afectado el uso de anticonceptivos en general y de algunos en particular.

Métodos: Las pautas de uso de anticonceptivos se determinan en base a los datos obtenidos en las encuestas nacionales y los niveles de acceso a cuatro métodos (esterilización femenina, el DIU, la píldora y el condón) son medidos de acuerdo con el porcentaje estimado de parejas para las cuales cada método se encontraba disponible en 1982, 1989, 1994 y 1999. El análisis se centra en la relación que existe entre el acceso a los anticonceptivos y las pautas de uso.

Resultados: En los cuatro ciclos del estudio de esfuerzo del programa, la prevalencia media de los cuatro métodos aumenta de acuerdo con el promedio de acceso. Por ejemplo, la prevalencia media en 1994 y 1999 fue de cerca del 12% en los países donde el acceso era muy bajo, en comparación con el 44% en aquellos que ofrecían un acceso elevado. La prevalencia presentó su más alto nivel en los países donde el acceso a todos los métodos era uniformemente elevado. En 1994, por ejemplo, la prevalencia media fue del 12% en países donde la disponibilidad media era elevada pero la diversidad en la disponibilidad de determinados métodos era baja, en comparación con una prevalencia del 9% en los países donde la disponibilidad media era elevada y el acceso a determinados métodos variaba considerablemente. Entre 1982 y 1994, el número de países con un acceso elevado uniforme aumentó de nueve a 23, en tanto que el número con acceso uniformemente bajo disminuyó de 23 a nueve. En los más bajos niveles de disponibilidad media, el condón y la píldora contribuyeron en mayor medida a la disponibilidad (40% y 36%, respectivamente), aunque al más elevado nivel, las contribuciones de los cuatro métodos se igualaron en 22-27% cada uno. La situación con respecto a la prevalencia es similar: el porcentaje que le corresponde a la píldora al más bajo nivel es del 67%, en comparación con el 31% al más alto nivel, donde lo supera la esterilización femenina (36%).

Conclusiones: En muchos países aún no se ha logrado disponer de una amplia gama de anticonceptivos. Esta carencia restringe el acceso personal a cada método, así como el uso de anticonceptivos en general. Hasta el punto que la posibilidad de optar por una protección anticonceptiva satisfactoria depende del fácil acceso a métodos múltiples, existe un claro mandato de prestar una mayor atención programática a contar con una amplia gama de métodos.

RÉSUMÉ

Contexte: Pour que chacun puisse bénéficier d'un choix d'options contraceptives, une gamme de méthodes doit être aisément accessible. Les mesures d'accès démontrent cependant de graves lacunes, au détriment de la pratique de chaque méthode. Le nombre de méthodes proposées et la mesure de leur disponibi-

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lité différent d'un pays à l'autre. L'évolution de ces facteurs au fil du temps et leurs effets sur la contraception en général et sur la pratique de méthodes individuelles doivent être documentés.

Méthodes: Les tendances de la pratique contraceptive sont dérivées des données d'enquêtes nationales, et les niveaux d'accès à quatre méthodes (la stérilisation féminine, le stérilet, la pilule et le préservatif) sont mesurés par estimation de la proportion des couples pour lesquels chaque méthode est disponible, à compter de 1982, 1989, 1994 et 1999. L'analyse se concentre sur le rapport entre l'accès aux contraceptifs et les tendances d'usage.

Résultats: Aux quatre cycles de l'étude d'effort programmatique, la prévalence moyenne des quatre méthodes augmente en même temps que l'accès moyen. Ainsi, la prévalence, en 1994 et 1999, était proche de 12% dans les pays caractérisés par un accès très limité, par rapport à 44% dans ceux offrant un accès très élevé. La prévalence atteint les plus hauts niveaux dans les pays où l'accès à toutes les méthodes est uniformément élevé. En 1994, par exemple, la prévalence moyenne était de 12% dans les pays à disponibilité moyenne élevée et faible diversité de méthodes individuelles, par rapport à 9% dans ceux où la disponibilité moyenne était élevée mais où l'accès aux méthodes individuelles était largement variable. Entre 1982 et 1994, le nombre de pays offrant un accès uniformément élevé est passé de neuf à 23, tandis que le nombre de ceux présentant un accès

uniformément faible baissait, de 23 à neuf. Au plus faible niveau de disponibilité moyenne, le préservatif et la pilule contribuent le plus à la disponibilité (40% et 36%, respectivement), mais au niveau supérieur, la contribution des quatre méthodes s'égalise, entre 22 et 27% chacune. On observe une situation semblable pour la prévalence: la part de la pilule au plus faible niveau de disponibilité est de 67%, par rapport à 31% au plus haut niveau, où la stérilisation féminine la surpasse (36%).

Conclusions: L'offre d'un choix complet de contraceptifs variés n'est pas encore atteinte dans de nombreux pays. Cette absence limite l'accès personnel à chaque méthode aussi bien que la pratique globale des méthodes au sein de la population. Dans la mesure où la capacité de choisir une protection contraceptive satisfaisante dépend d'un accès aisé à une multiplicité de méthodes, les programmes se doivent clairement d'accorder une plus grande attention à la fourniture d'une gamme complète de méthodes.

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CALL FOR PAPERS

The legal status of abortion varies widely around the world, but health care providers in all countries share a need for information on treatment for complications from spontaneous or induced abortion. In response to this need, the September 2003 issue of *International Family Planning Perspectives* will include a special section on postabortion care as part of the journal's "Issues in Perspective" series. We are seeking papers on provision of postabortion care; integration of family planning counseling and services with postabortion care; the technology, training and costs involved in initiating services; quality of care; and access issues. We will consider commentaries as well as qualitative and quantitative research.

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Two randomized controlled trials comparing the Tubal Ring and Filshie Clip for tubal sterilization

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Rosalie Dominik, M.P.H., and the Clinical Investigator Team

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Objective: To compare the effectiveness and safety of the Filshie Clip and Tubal Ring systems when applied via minilaparotomy and laparoscopy.

Design: Prospective, multicenter randomized controlled clinical trial, with postoperative evaluation by a physician who was masked to the operative technique.

Setting: Healthy volunteers in a variety of hospital settings.

Patient(s): 2746 women (915 in the minilaparotomy study and 1831 in the laparoscopy study) who had requested permanent surgical sterilization.

Intervention(s): Surgical tubal ligation, using either Filshie Clips or Tubal Rings. A physician other than the surgeon evaluated the patients after the operation and again at 1, 6, and 12 months after surgery.

Main Outcome Measure(s): Pregnancy rates and safety-related events.

Result(s): During the 12 months after surgery, two women who received the Filshie Clip and two women who received the Tubal Ring became pregnant, giving a 12-month life-table pregnancy probability of 1.7 per 1000 women in both groups. The Tubal Ring was more difficult to apply and had higher rates of tubal or mesosalpingeal injuries at surgery. The Filshie Clip group had three cases of spontaneous clip expulsion during the follow-up period.

Conclusion(s): Both the Filshie Clip and Tubal Ring are effective and safe for use in tubal occlusion. (Fertil Steril® 2000;74:525-33. ©2000 by American Society for Reproductive Medicine.)

Key Words: Tubal occlusion devices, female sterilization, Filshie Clip, Tubal Ring

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In 1996 the U.S. Food and Drug Administration approved the Filshie Clip for tubal sterilization. The Filshie Clip and Tubal Ring differ substantially in their mode of action. The Tubal Ring uses a special applicator to draw up 2 to 3 cm of the fallopian tube through a stretched tubal ring (1). The Tubal Ring is then released at the base of this loop, where it constricts tightly, cutting off the circulation to the loop of fallopian tube. This causes tissue necrosis, followed by healing and fibrosis, leading to permanent tubal occlusion.

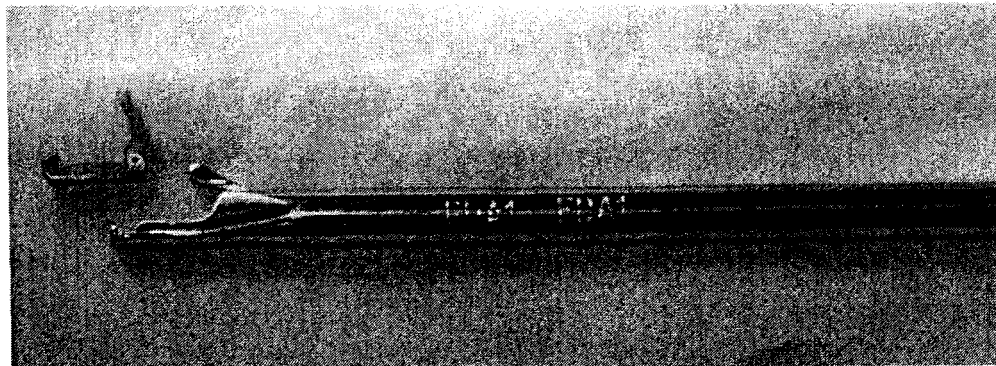
The Filshie Clip is a hinged device made of titanium lined with silicone rubber (Figure 1). The pressure exerted by the applicator closes the clip around the fallopian tube and flattens the curved upper jaw of the clip (2). This action causes the upper jaw's leading edge to extend under the lip of the lower jaw, locking it into

position; this simultaneously traps and occludes the fallopian tube. With the use of a Filshie Clip, only the part of the tube that is compressed between the jaws of the clip—about 4 mm—is damaged.

Published reports of failure rates with the Filshie Clip and the Tubal Ring have varied widely. This may reflect several factors, including the level of experience of the surgeon, the timing of the surgery (postpartum or interval), the procedure used, the method used to calculate the failure rates, and the characteristics of the study populations (3-8). To evaluate clinically the relative effectiveness and safety of the two methods, we conducted two randomized controlled trials of the Filshie Clip and Tubal Ring for cases of interval sterilization. One study compared the devices when they were applied via mini-

FIGURE 1

Filshie Clip and applicator.



Sokal. Filshie Clip vs. Tubal Ring. Fertil Steril 2000.

laparotomy and the other when they were applied via laparoscopy.

MATERIALS AND METHODS

Except for the type of surgical approach used (laparoscopy or minilaparotomy), the two study protocols were identical. The investigators/operators at each site were required to be experienced surgeons.

The Family Health International (FHI) institutional review board approved the two protocols on June 1, 1984. Each study center obtained approval to conduct the study from its own institutional review board prior to the study's initiation. If a local institutional review board was not available, FHI's board acted in lieu of a local board.

Women who were at least 21 years of age, legally able to consent to sterilization, and had a normal physical and pelvic examination were eligible to participate in the studies. We did not enroll women if they had undergone a pregnancy termination (either a delivery or abortion) within the past 42 days or if they had a preexisting clinically important abnormal condition such as diabetes, or renal or cardiac disease. We excluded women who showed evidence of significant pelvic pathologic conditions during the physical examination. We did not enroll women who were already pregnant or women who were undergoing surgery other than a routine curettage or IUD removal concurrent with the sterilization procedure. For example, a woman was not eligible if she was coming in for both an induced abortion and a sterilization procedure. Nor did we enroll women who required sterilization for reasons other than voluntarily limiting the size of her family.

After each participant signed an informed consent agreement, we randomized her to receive one of the two tubal occlusion devices; this process was performed with the use

of a computer-generated randomization scheme stratified by center. The woman's group assignment was then revealed to the surgeon by means of a sealed, sequentially numbered, opaque envelope that was provided to the site at the study's initiation by FHI. In one study, which was carried out at five centers, minilaparotomy was used to access and view the fallopian tubes; in the other study, which was carried out at seven centers, laparoscopy was used.

Prior to surgery, we took a medical history and conducted a physical examination, including a pelvic examination, for each woman. The surgeon recorded the type of anesthetic, the surgical approach, and the reason for any change from the assigned tubal occlusion method if applicable. Before each woman was discharged, another physician, who was not informed of the type of clip the woman had received, assessed her for complications involving the surgical incision, pelvic pain and infection, and any other complications or complaints.

Another physician (again, someone other than the surgeon) evaluated the participants at 1, 6, and 12 months after their sterilization procedure. At selected sites, a 24-month evaluation was planned for a subset of laparoscopy participants. At the early (1-month) follow-up visit, we evaluated the women for complications associated with the surgical procedure. At the later visits, we gave participants a physical examination that included a pelvic examination and a clinical assessment of pelvic infection, and asked them questions about their menstrual patterns (including intermenstrual bleeding and pain). At all follow-up visits, we recorded pregnancies, adverse events, abdominal or pelvic surgery, or hospital admissions that had occurred since the surgery. If clinical signs of pregnancy were suspected, we diagnosed pregnancies with a urine pregnancy test, pelvic examination, or other clinical evaluation. We did not routinely administer a chemical pregnancy test at the 12- or 24-month visits.

A total of five centers from five countries were included in the minilaparotomy trial and a total of seven centers from five countries were included in the laparoscopy trial. Recruitment at most centers began in 1984 or 1985. Each center was monitored per Food and Drug Administration guidelines, and fieldwork was completed at most centers by 1989, and at the last center in February 1990.

We defined three different subject populations before we analyzed the individual trial results. The intent-to-treat population included all women who were assigned to receive the Filshie Clip or the Tubal Ring. The treated population included all women who had at least one fallopian tube occluded with either a Filshie Clip or a Tubal Ring. When a surgeon was unable to apply a Filshie Clip or Tubal Ring, he used an alternate method, most commonly a partial salpingectomy. In two cases where the tubal ring was assigned no sterilization procedure was performed on one tube because a gross tubal pathologic condition was observed.

The efficacy population included all women who had both fallopian tubes occluded with their assigned device except those who had inclusion criteria violations that might interfere with the evaluation of effectiveness. Prior to initiation of the primary analysis for either trial, we determined the treated population to be the primary analysis population of interest. The treated population is the focus of the individual trial and pooled trial results presented here.

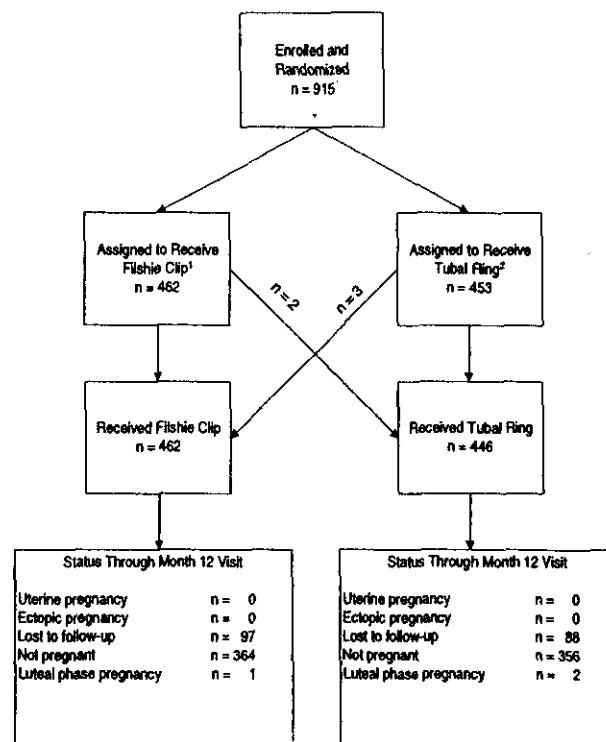
The effectiveness outcome of interest was pregnancy. We calculated 12-month gross cumulative life-table pregnancy probabilities by device type (combining the data collected in the two studies), and by device type within each study (9). We calculated standard errors using the method described by Peto et al. (10). We used a log-rank test ($\alpha = 0.05$) to test for differences in pregnancy curves by device group (11). We also calculated gross cumulative life-table pregnancy probabilities through 24 months for the subgroup of participants for whom extended follow-up observations were planned. We excluded women from the effectiveness analysis for the treated population who were later determined to have been pregnant at the time their tubes were occluded (i.e., women with luteal phase pregnancies).

Women who had a hysterectomy or other surgical intervention that would alter the risk of pregnancy were censored from the life-table analysis. Participants who were not reported to be pregnant were censored from the life-table analysis as of the date of their last visit. For pregnancies, the date of conception was estimated using an algorithm based on LMP and gestational age at termination or pregnancy confirmation.

We calculated the percentage of surgical injuries and primary incision complications, of infections, and of other major complications at the early follow-up examination, by sterilization device received, within strata defined by the surgical approach. Within each surgical approach stratum,

FIGURE 2

Participant flow chart for the minilaparotomy study.



¹Includes 1 woman who received other occlusion techniques on both tubes who is excluded from subsequent counts.

²Includes 6 women who received other or no occlusion techniques on both tubes who are excluded from subsequent counts.

Sokal. *Filshie Clip vs. Tubal Ring. Fertil Steril 2000.*

we used Fisher's exact test ($\alpha = 0.05$) to test for differences between device groups in the number of women having each type of event. We did not combine early safety results for the two surgical approaches because of differences in the procedures. We summarized the reports of hospital readmission and subsequent abdominal or pelvic surgery during the follow-up observation.

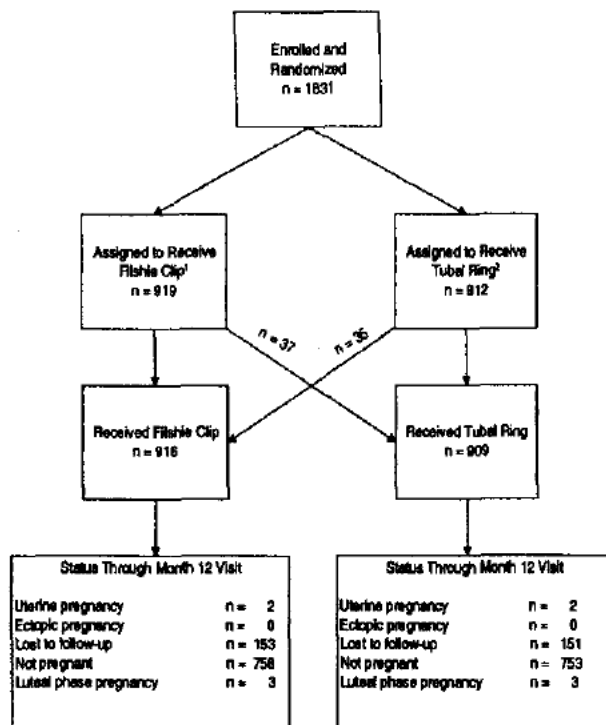
RESULTS

Unless otherwise stated, we present results for the treated population. A total of 2746 women (915 in the minilaparotomy study and 1831 in the laparoscopy study) comprised the intent-to-treat population (Figs. 2 and 3). Of these, we assigned 1381 to the Filshie Clip and 1365 to the Tubal Ring. We identified major violations of the inclusion/exclusion criteria in 80 women (59 in the minilaparotomy study and 21 in the laparoscopy study). Of these, 30 had received the Filshie Clip and 41 had received the Tubal Ring. Nine women received neither study device. About one-third (27) of the protocol violations were women whose last pregnancy

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FIGURE 3

Participant flow chart for the laparoscopy study.



¹ Includes 1 woman who received no occlusion technique on either tube who is excluded from subsequent counts.

² Includes 1 woman who received a Tubal Ring on one tube and a Filshie Clip on the other, and 4 women who received either or no occlusion techniques on both tubes who are excluded from subsequent counts.

Sokal. *Filshie Clip vs. Tubal Ring. Fertil Steril 2000.*

had been terminated less than 5 weeks before surgery. Among the other protocol violations were 16 women with preexisting pelvic pathologic conditions. The 37 other violations consisted of a variety of preexisting conditions. Table 1 shows the number of women by analysis population, surgical approach, and country.

The women in both device groups had a mean age of 31 years (± 0.133 SE Filshie Clip and ± 0.129 SE Tubal Ring) and had given birth to an overall average of 3.7 children. About one-third of the women in both groups had been pregnant within 6 months prior to sterilization and about 70% had used some form of contraceptive method in the 3 months prior to sterilization. About one-third of the women in each group reported that they had not had menses during the 3 months prior to enrollment. In both groups, the likelihood of amenorrhea at baseline was considerably higher among women who had delivered within the 6 months preceding study enrollment than among other women, presumably due to breast feeding. In both device groups fewer

TABLE 1

Number of participants in each analysis population by device group.

Analysis population, study and country	Filshie Clip	Tubal Ring
Intent-to-treat population ^a	1381	1365
Minilaparotomy study	462	453
Panama	149	150
Peru	100	100
Kenya	67	64
Brazil	51	47
Mexico	95	92
Laparoscopy study	919	912
Panama	150	150
Indonesia ^b	149	149
Thailand ^c	383	375
Mexico	109	110
Dominican Republic	128	128
Treated population ^d	1378	1355
Minilaparotomy study	462	446
Laparoscopy study	916	909
Efficacy population ^d	1300 ^e	1264 ^f
Minilaparotomy study	431	403
Laparoscopy study	869	861

^a By assigned device.

^b One of the two centers in Indonesia enrolled 150 participants and the other enrolled 148 participants.

^c One of the two centers in Thailand enrolled 458 participants and the other enrolled 300 participants.

^d By device received.

^e This group is a subset of the treated population excluding 78 women: 30 women with violations of inclusion/exclusion criteria, 4 women with luteal phase pregnancies, 37 women who received a device other than the device indicated on the randomization schedule provided to the site, and 7 other women who did not receive the assigned device on both tubes due to technical failures.

^f This group is a subset of the treated population excluding 91 women: 41 women with violations of inclusion/exclusion criteria, 5 women with luteal phase pregnancies, 39 women who receive a device other than the device indicated on the randomization schedule provided to the site (one of these women was also among the 41 with a protocol violation), and 7 other women who did not receive the assigned device on both tubes due to technical failures.

Sokal. *Filshie Clip vs. Tubal Ring. Fertil Steril 2000.*

than 10% reported previous intraperitoneal surgery and 2-3% reported past pelvic inflammatory disease.

Operators experienced some type of surgical difficulty when operating on 7% of the women assigned to receive the Filshie Clip and 8% of the women assigned to receive the Tubal Ring in the intent-to-treat population. The four most common surgical difficulties in the minilaparotomy study were 1) visualizing the tube (20 Filshie Clip cases and 22 Tubal Ring cases); 2) grasping the tubes (9 Filshie Clip and 14 Tubal Ring); 3) entering the peritoneum (5 Filshie Clip and 9 Tubal Ring); and 4) occluding the tubes (1 Filshie Clip and 10 Tubal Ring). The four most common difficulties in

TABLE 2

Six- and 12-month gross cumulative life-table pregnancy probabilities per 1000 women by approach and device group, treated population.

Approach	Month	Filshie Clip			Tubal Ring			P value ^c
		At risk ^a	Cumulative probability of pregnancy ^b	Standard error	At risk ^a	Cumulative probability of pregnancy ^b	Standard error	
Both approaches combined	6	1238	0.8	(0.82)	1211	0.8	(0.82)	.98
	12	1111	1.7	(1.33)	1091	1.7	(1.35)	
Laparoscopy	6	822	1.2	(1.23)	818	1.2	(1.23)	.99
	12	749	2.5	(1.99)	738	2.5	(2.01)	
Minilaparotomy	6	416	0.0	—	393	0.0	—	—
	12	362	0.0	—	353	0.0	—	

^a Number of women remaining in the trial at the beginning of the month.

^b Per 1000 women.

^c Log-rank test for comparison of 12-month pregnancy curves.

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the laparoscopy study were 1) grasping the tubes (14 Filshie Clip and 10 Tubal Ring); 2) entering the peritoneum (13 Filshie Clip and 6 Tubal Ring); 3) visualizing the tube (11 Filshie Clip and 6 Tubal Ring); and 4) occluding the tubes (8 Filshie Clip and 7 Tubal Ring).

Operators also reported details of the following less common difficulties. With the Tubal Ring an operator reported transection of the tube, followed by application of a second ring, and suturing of the mesosalpinx for hemostasis. Another operator reported application of a second ring to the right tube due to difficulties with the first ring, along with freeing up of adhesions to the ovary on the same side. With the Filshie Clip, one operator reported that a Filshie Clip broke during application. The pieces were removed from the abdomen. Another operator reported a Filshie Clip that did not close properly. It was replaced by another clip.

Operators failed to apply the assigned device to both fallopian tubes in a total of 114 women. One center generated their own randomization schedule rather than using the one provided by FHI, resulting in 68 women (34 per group) receiving a device other than the device on the list FHI generated. In a total of 37 cases (6 assigned to the Filshie Clip and 31 assigned to the Tubal Ring), problems encountered during surgery prevented application of the assigned device to both tubes. In 11 of these 37 cases, operators reported adhesions as the problem preventing application of the Tubal Ring. In five other cases where the Filshie Clip was assigned and in four other cases where the Tubal Ring was assigned, the operators applied a device other than the assigned device. The operators provided no explanation for the inconsistency, and these occurrences appeared to be due to unintentional error.

Within each trial, the days until discharge did not vary by

device. In the laparoscopy study, 84% of the women were discharged from the clinic on the day of surgery; whereas 63% of those in the minilaparotomy study were discharged on the day of surgery.

The percentage of women returning for follow-up visits was similar in the two groups. Over 90% of the women in each device group returned for an early follow-up evaluation, and about 82% in each group completed a 12-month or later visit. Among the subset of laparoscopy participants for whom 24-month follow-up observation was planned (356 women in the Filshie Clip group and 347 women in the Tubal Ring group), about 70% returned 684 or more days after surgery.

Table 2 shows the 6- and 12-month cumulative life-table pregnancy probabilities. There were two pregnancies in each group. All four pregnancies were intrauterine, and all occurred among women in the laparoscopy study. Given the final sample size and the observed discontinuation rate, the study provided about 56% power to detect a difference between annual pregnancy probabilities of 2 per 1000 and 8 per 1000 (12).

The numbers "at risk" in month 12 in Table 2 are slightly less than the numbers of nonpregnant women in Figures 2 and 3 who made 12-month visits. These differences reflect the use of slightly different definitions. A 12-month visit had been defined as any visit between 318 and 442 days after surgery. However, for the life-table analysis, women were at risk for pregnancy at month 12 only if they had a visit on day 336 or later (i.e., the first day of the 12th month after surgery).

In the subset of laparoscopy study participants who were to be observed for 24 months, one additional pregnancy

TABLE 3

Surgical injuries and safety events reported at early follow-up observation, treated population.

Safety Event	Minilaparotomy				Laparoscopy			
	Filshie		Tubal Ring		Filshie		Tubal Ring	
	N	(%)	N	(%)	N	(%)	N	(%)
Surgical injuries								
None	435	(94.2)	406	(91.0)	904	(98.7)	880	(96.8)
Cervical laceration	1	(0.2)	4	(0.9)	6	(0.7)	3	(0.3)
Uterine perforation	4	(0.9)	3	(0.7)	3	(0.3)	2	(0.2)
Tubal/mesosalpingeal injury	18	(3.9)	29	(6.5)	2	(0.2)	23	(2.5)
Bladder injury	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Other	4	(0.9)	4	(0.9)	0	(0.0)	1	(0.1)
Total	462	(100.0)	446	(100.0)	916	(100.0)	909	(100.0)
<i>P</i> value ^a			0.08				0.01	
Primary incision complications at early follow-up								
None	334	(86.3)	314	(85.8)	739	(95.8)	742	(95.2)
Serious discharge	8	(2.1)	7	(1.9)	20	(2.6)	22	(2.8)
Inflammation	20	(5.2)	14	(3.8)	2	(0.3)	8	(1.0)
Abscess	1	(0.3)	2	(0.6)	1	(0.1)	0	(0.0)
Bleeding	0	(0.0)	2	(0.6)	3	(0.4)	1	(0.1)
Hematoma	11	(2.8)	5	(1.4)	0	(0.0)	2	(0.3)
Wound dehiscence	10	(2.6)	13	(3.6)	3	(0.4)	4	(0.5)
Other	3	(0.8)	9	(2.5)	3	(0.4)	0	(0.0)
Total	387	(100.0)	366	(100.0)	771	(100.0)	779	(100.0)
<i>P</i> value ^a			0.92				0.62	
Infections at early follow-up								
None	383	(99.0)	363	(99.2)	770	(99.9)	773	(99.2)
In uterus	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
In adnexa	0	(0.0)	2	(0.6)	0	(0.0)	1	(0.1)
Other	3	(0.8)	1	(0.3)	1	(0.1)	4	(0.5)
Total	387	(100.0)	366	(100.0)	771	(100.0)	779	(100.0)
<i>P</i> value ^a			1.00				0.12	
Other major complications at early follow-up^b								
None	382	(98.7)	360	(98.4)	763	(99.0)	771	(99.0)
At least one	5	(1.3)	6	(1.6)	8	(1.0)	8	(1.0)
Total	387	(100.0)	366	(100.0)	771	(100.0)	779	(100.0)
<i>P</i> value ^a			0.77				1.00	

^a By Fisher's exact test, any complication event versus no event.^b Specifically, urinary tract infection, vaginal bleeding other than menses/lochia, respiratory, cardiovascular, gastrointestinal, drug allergy, and other were the precoded responses provided in the other major complication section of the early follow-up visit data collection form.Sokal. *Filshie Clip vs. Tubal Ring. Fertil Steril* 2000.

occurred in the Filshie Clip group. The 12- and 24-month cumulative pregnancy probabilities were 3.0 and 6.8 per 1000 women, respectively, for the Filshie Clip group and 3.0 and 3.0 for the Tubal Ring group ($P = .58$ for the comparison through 24 months).

Two additional pregnancies were reported after the end of the 12-month follow-up period, among women in the 12-month minilaparotomy study. Because their estimated dates of conception were greater than 12 months since surgery, they were not included in the life-table analysis. One pregnancy occurred in the Filshie Clip group and one in the Tubal

Ring group. The pregnancy in the Tubal Ring group was ectopic.

Thus a total of six intrauterine pregnancies and one ectopic pregnancy were reported as poststerilization events in the overall study population: four in the Filshie Clip group and three (including the ectopic) in the Tubal Ring group. Other pregnancies identified during the study which were not considered sterilization failures included two ectopic pregnancies diagnosed in Filshie Group patients and one in a Tubal Ring patient during the sterilization procedure itself. In addition, nine luteal phase pregnancies, defined as con-

ception occurring on or before the date of the sterilization procedure, were diagnosed during the follow-up period (four in the Filshie Clip group and five in the Tubal Ring group).

In the minilaparotomy study, the number of participants with surgical injuries was similar for the two device groups (Table 3). In the laparoscopy study, significantly more participants in the Tubal Ring group than in the Filshie Clip group were reported to have surgical injuries ($P = .01$). These were primarily tubal/mesosalpingeal injuries. Among the nine "other" surgical injuries shown in Table 3, the only notable event we observed was a cardiac arrest in a Filshie Clip participant in the minilaparotomy study. This event was ascribed to a vasovagal reaction. The patient was successfully resuscitated and was discharged 2 days later with no further complications at long-term follow-up.

Within each study, the number of participants with primary incision complications, infections, and other complications at early follow-up was similar for the two device groups (see Table 3).

During the scheduled 12- or 24-month follow-up period after sterilization, 15 women in the Filshie Clip group and 20 women in the Tubal Ring group were hospitalized or underwent abdominal or pelvic surgery. Most were unrelated to the sterilization procedure. There were no clinically significant differences between the two groups in the indications for surgery or hospitalization.

Not included in the complications noted above were three cases of Filshie Clip expulsions, two of which occurred after the planned follow-up period. None of these women required hospitalization, but one woman subsequently underwent a diagnostic laparoscopy. This woman reported an asymptomatic expulsion of a Filshie clip from the rectum 18 months after the sterilization procedure. She reported that she noticed the clip because she was in the habit of routinely examining her stool in the toilet to look for parasites, a habit that her mother had taught to her as a child. After the expulsion, she underwent a diagnostic laparoscopy, and a granulomatous adhesion was noted between the fallopian tube and the descending colon. The woman was asymptomatic before and after the expulsion.

Another woman passed a Filshie Clip from the urethra 10 months after sterilization. Prior to the expulsion, she reported lower abdominal pain and the desire to urinate. A third woman had a Filshie Clip expelled from the vagina 34 months after the sterilization procedure. Four and a half months prior to the expulsion, she had undergone an abdominal hysterectomy. Following the hysterectomy, she had reported vaginal spotting and pain on deep penetration during intercourse. She had been examined for this complaint, and a small granulomatous area was noted in the vaginal vault but not treated. She had no symptoms following the expulsion.

In two other cases, surgeons reported that Filshie Clips were displaced from the fallopian tube. These observations

were made during surgery for pelvic pain 6 years after sterilization, and for chronic salpingitis 30 months after sterilization, respectively. Two deaths occurred during the study, both unrelated to the sterilization procedure: one was due to an automobile accident, and the other due to a metastatic lymphoma.

DISCUSSION

Pregnancy Rates

Our estimate of the probability of pregnancy through the first year after sterilization with the Tubal Ring (1.7 per 1000) was lower than the probability (5.9 per 1000 women) observed in the Centers for Disease Control and Prevention (CDC) U.S. Collaborative Review of Sterilization (CREST) (8). In our trials, the sterilization procedures were performed by a small number of investigators selected because of their surgical expertise and experience. In the CREST study, resident physicians at teaching centers performed the sterilization procedures. The CREST study authors noted this limitation regarding the generalizability of their results. Procedures done by resident physicians in a teaching program have been shown to lead to higher pregnancy rates (4, 13). Thus, the lower pregnancy rates we observed may be due to the choice of more experienced investigators as operators.

Alternatively, differences in estimates of the risk of pregnancy may be due to differences in the underlying fecundity of the study populations, incomplete follow-up observations, or chance. The age distributions for the women in our study and the 3329 women in the "silicone rubber band" group of the CREST study were similar, and Tubal Ring recipients in both of the studies included only women who desired interval sterilization. Our study did include a substantial proportion of women who were reported to be amenorrheic since their previous delivery (presumably due to breastfeeding), but comparable data were not provided for the CREST study. It should be noted that the "spring clip" that was studied in the CREST study was the Wolf Clip (also known as the Hulka Clip), not the Filshie Clip. The Filshie Clip was not available in the United States when the CREST study was conducted.

The number of women that we observed for 24 months was small. At the time this study was conducted—well before the CREST study results were reported—it was believed that most failures of surgical sterilization would become apparent within a year.

Our study was limited to interval sterilizations, rather than postpartum sterilizations. Both of these devices may be harder to use and/or less effective in the immediate postpartum period, although not all surgeons agree (14, 15).

Censoring participants as of the date of their last visit would be expected to slightly underestimate the 12-month pregnancy probabilities, because pregnancies that were not yet clinically evident could have been missed. We performed an analysis that censored women who had not become preg-

nant 60 days prior to their last visit. The impact on the point estimate of the pregnancy probabilities was quite small. For the Filshie Clip group the estimate went from 1.70 per 1000 women to 1.76 per 1000 women. For the Tubal Ring group the estimate went from 1.68 per 1000 women to 1.72 per 1000 women.

On the other hand, women who become pregnant after sterilization are likely to notify their physicians about such a pregnancy, even after the formal end of a study. In fact, as noted in the results, we received reports from investigators about two such pregnancies.

Adverse Events

Serious adverse events related to sterilization with either device were rare. The choice of surgical approach did not appear to affect the overall efficacy or safety. Both of the study devices have specific advantages and disadvantages. The Filshie Clip destroys less of the fallopian tube than the Tubal Ring, which may facilitate surgical reversal. The Filshie Clip is associated more commonly with clip-related adverse events, whereas the Tubal Ring leads to more frequent tubal or mesosalpingeal injuries.

Clip-related adverse events (expulsion, or abscess or granuloma formation) are generally uncommon. The three clip expulsions we report are an unusual number. No other expulsions were reported among slightly over 4000 women in other Filshie Clip trials conducted by FHI (16). However, we have found published case reports of similar events: two women had abscess formation involving Filshie Clip migration into the inguinal canal (17, 18); one woman had a pelvic abscess associated with the Filshie Clip (19); one woman had a spontaneous expulsion via the urinary bladder (20); and one woman had a case of appendicitis attributed to Filshie Clip migration (21). One of the expulsions reported in this trial happened after a hysterectomy. Another author has reported two similar events involving Wolf Clips, and recommended that any tubal clips should be removed at the time of hysterectomy (22).

The Wolf Clip, also known as the Hulka Clip, is similar in size to the Filshie Clip. In the published literature regarding the Wolf Clip, there are reports of two other women who had Wolf Clip expulsions and three women who had abscess or granuloma formation (23–26). We have not found any similar reports in the literature concerning spontaneous expulsion of Tubal Rings. However, given the much smaller size of the Tubal Ring and the almost asymptomatic character of clip expulsions, it is possible that unnoticed Tubal Ring expulsions may have occurred. We are unaware of any reports of confirmed abscess formation involving the Tubal Ring; however, adnexal masses in two women that resolved following antibiotic treatment have been reported (26).

The finding of significantly more frequent tubal or mesosalpingeal injuries with the Tubal Ring is probably an intrinsic characteristic of its mode of operation. The use of

the Tubal Ring requires the operator to draw a loop of about 2 cm of the fallopian tube into a metallic tube that is part of the applicator. The Tubal Ring is then slipped over the base of the loop and the fallopian tube is released. In a series of 2299 patients, Yoon and Poliakoff reported a 3.3% incidence of tubal transections, and a 0.7% incidence of mesosalpingeal hematoma (1). More surgical difficulties in “occluding the tube” (21 vs. 9) and more cases of inability to apply the assigned device to both tubes (31 vs. 6) were reported with the Tubal Ring than with the Filshie Clip. These differences may reflect an intrinsic characteristic of the application of the Tubal Ring, in that its application requires greater access to and mobility of a longer piece of the fallopian tube compared to the Filshie Clip.

Loss to Follow-Up Observation

Our pooled loss-to-follow-up rates at the 12-month visit were 18.1% for the Filshie Clip group and 17.6% for the Tubal Ring. In comparison, the CREST study, a prospective, multicenter cohort study conducted in the United States, had a loss to follow-up of only 11% at the 1-year interview (8).

The effect of the loss to follow-up on our conclusions depends on two factors: 1) whether loss to follow-up is correlated with the risk of pregnancy, and 2) whether loss to follow-up was different for one device versus the other. We cannot estimate the risk of pregnancy in the women who were lost to follow-up observation, but we did compare the characteristics of those women by treatment group (data not shown). We found that the women lost to follow-up observation in both groups were similar. This suggests that, although our estimate of the absolute pregnancy rates could be too high or too low, our comparison of the two devices' efficacy should be fair and unbiased.

Conclusion

Though they have slightly different clinical profiles, both the Filshie Clip and Tubal Ring are effective and safe for use in tubal occlusion.

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Contraceptive Failure, Method-Related Discontinuation And Resumption of Use: Results from the 1995 National Survey of Family Growth

By James Trussell and Barbara Vaughan

Context: Half of all pregnancies in the United States are unintended. Of these, half occur to women who were practicing contraception in the month they conceived, and others occur when couples stop use because they find their method difficult or inconvenient to use.

Methods: Data from the 1995 National Survey of Family Growth were used to compute life-table probabilities of contraceptive failure for reversible methods of contraception, discontinuation of use for a method-related reason and resumption of contraceptive use.

Results: Within one year of starting to use a reversible method of contraception, 9% of women experience a contraceptive failure—7% of those using the pill, 9% of those relying on the male condom and 19% of those practicing withdrawal. During a lifetime of use of reversible methods, the typical woman will experience 1.8 contraceptive failures. Overall, 31% of women discontinue use of a reversible contraceptive for a method-related reason within six months of starting use, and 44% do so within 12 months; however, 68% resume use of a method within one month and 76% do so within three months. Multivariate analyses show that the risk of contraceptive failure is elevated among low-income women and Hispanic women. Low-income women are also less likely than other women to resume contraceptive use after discontinuation.

Conclusions: The risks of pregnancy during typical use of reversible methods of contraception are considerably higher than risks of failure during clinical trials, reflecting imperfect use of these methods rather than lack of inherent efficacy. High rates of method-related discontinuation probably reflect dissatisfaction with available methods.

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Unintended pregnancy is a major public health problem that affects not only the individuals directly involved but also society.¹ Half (48%) of all pregnancies in the United States are unintended: There were three million in 1994, the last year for which data are available. Half (48%) of all women aged 15–44 have had at least one unintended pregnancy.²

Most couples who want to avoid pregnancy practice contraception. Nevertheless, half (53%) of women with unintended pregnancies were using a family planning method in the month they conceived.³ Many of these women may have become pregnant because their method was not highly effective or was difficult for them to use consistently and correctly.

In the analyses described in this article, we used data from the 1995 National Survey of Family Growth (NSFG) to estimate life-table probabilities of contraceptive failure (pregnancy during contraceptive use) during typical use, of discontinuation for a method-related reason and of resumption of contraceptive use after discontinuation of a reversible method. We present estimates of contraceptive failure and discontinuation separately for each reversible method. However, separate es-

timates of resumption of use following method discontinuation for any reason are shown only for the pill, the male condom and sterilization; all other methods are combined in one category.

We also examined risk factors for contraceptive failure, contraceptive discontinuation for a method-related reason and resumption of contraceptive use after discontinuation of the prior method. Finally, we estimated the number of contraceptive failures the typical woman would experience in her lifetime.

Our analyses of contraceptive failure and discontinuation of contraceptive use for a method-related reason fit squarely into a rich substantive and methodological literature on these subjects. This article breaks new ground in four respects. First, we have expanded the standard set of risk factors for contraceptive failure (method, age, race and ethnicity, parity, income, previous method and desire for children in the future) to include two new time-varying factors: current marital status and current work or study status. Second, we systematically examined this set of nine factors to determine their effects on the risk of discontinuation for a method-related reason. Third, we examined re-

sumption of contraceptive use following discontinuation for any reason. Finally, we have presented a unified set of results for contraceptive failure, discontinuation for a method-related reason and resumption of use following discontinuation.

Data

The 1995 NSFG contains extremely detailed information about methods of contraception used by the 10,847 female respondents aged 15–44 during a focal period from January 1991 until their interview (at varying dates in late 1995).⁴ For instance, there are 17 questions about method use for each of the up to 58 months in the focal period; there are, however, no summary variables describing the beginning and ending dates of method use. There is similar detail in questions about periods of no exposure to risk of pregnancy, and about time spent in union; the codebook is more than 6,300 pages long.

Thus, the construction of even straightforward variables for analysis entails examination of many source variables. The complexity of the survey has also resulted in some deficiencies in the data quality, such as missing data caused by erroneous skip patterns or failure to include questions for some classes of respondents.

Defects in Discontinuation Data

The most serious problem in the NSFG data is the substantial underreporting of induced abortion. Estimates of the extent of underreporting can be obtained by comparing the number of abortions derived from surveys of abortion providers

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conducted by The Alan Guttmacher Institute with the number reported in the NSFG. The overall level of abortion underreporting in the 1995 NSFG for the four-year period 1991-1994 is estimated to be 55% in the main interview, 48% in the computer-assisted self-interview for sensitive topics and 41% when the main interview is combined with the self-report.⁵ It is likely that some induced abortions are misreported as spontaneous abortions,^{6*} but because others are not reported at all, the sum of reported induced and spontaneous abortions is without doubt too low.

The consequence, all else being equal, is an underreporting of contraceptive failure and perhaps of method-related discontinuation. It is likely that what appears in some instances to be continuous use of a contraceptive method in fact contains a contraceptive failure (an important cause of discontinuation) or that what appears to be a simple switch of methods in fact resulted from contraceptive failure.

Although attempts have been made to correct for such underreporting in the NSFG by using surveys of abortion patients to ascertain contraceptive use prior to the abortion,⁷ the correction for underreporting of abortion would tend to result in overestimates of contraceptive failure because women in abortion clinics probably overreport use of a contraceptive at the time of conception, thus shifting responsibility for the pregnancy from themselves (and their partner) to contraceptive failure.⁸

Likewise, in personal interviews for the NSFG, women probably tend to overreport contraceptive use at the time of an unintended conception. Evidence for this suspicion is provided by a first-year probability of pregnancy of 6% during use of the IUD (a method with little scope for user error) among married women in the 1976 and 1982 NSFGs. This probability is much higher than rates observed in clinical trials of IUDs⁹ (see Appendix for further evidence).

Thus, while induced abortions (and contraceptive failures leading to induced abortions) are underreported, contraceptive failures leading to reported conceptions are probably overreported. These two sources of bias operate in opposite directions and thus would tend to cancel each other; therefore, adjustment for underreporting of induced abortion would make the pregnancy rates too high.¹⁰

The effect of abortion underreporting on estimates of contraceptive discontinuation is not clear. If an abortion prompts a change of method that is reported, there will be no effect. If, in contrast, an unre-

ported abortion occurs during an interval of reported continuous contraceptive use of the same method, estimates of discontinuation will be biased downward.

Another deficiency in the data is that women who were pregnant at the time of the interview were not asked when the pregnancy began or when they expected to deliver. For pregnancies that resulted from contraceptive failure, this omission means that the date of failure cannot be ascertained. Therefore, in analyzing contraceptive failure and discontinuation, we have terminated our observation of all women in the 10th month prior to the interview to avoid the possibility of missing reported pregnancies that occurred during contraceptive use.

The dates of starting and stopping method use were recorded using both a monthly calendar and a computer-assisted personal interview (CAPI) questionnaire. For reasons that are not apparent, there is a pronounced tendency to report method use as beginning in January of the years in the calendar[†]: The number of women who report starting a new method in January of each of the calendar years is approximately double the number who report beginning in the adjacent December or February.[‡] The pattern is less apparent for stopping use, as both December and January appear to be preferred months. Duration of use appears to be much less heaped; there is a deficit of segments with duration 10, and a surplus with durations 11 and 12.

The reason for stopping is not indicated in the calendar but can usually be determined or imputed by cross-checking other variables for the woman, either in the main respondent file or in the related pregnancy interval file (see Appendix). Once we deduced the reason method use was stopped, we could categorize it as either method-related (changed method, contraceptive failure, stopped use while still exposed to the risk of unintended pregnancy) or not method-related (planning pregnancy, no exposure to risk). Using life-table methods, we then determined the proportion of women still continuing to use each contraceptive in each month following initiation of use. Therefore, we could not determine proportions continuing use beyond four years.

In earlier rounds of the NSFG, women who were using a method in the first month of the contraceptive calendar were asked when they had begun to use that method. In all previous rounds of the survey, therefore, we were able to calculate how long women had been using their

method at the time the calendar began and enter them into the life table at that duration. For the 1995 NSFG, a decision was made to drop that question, but in practice it was omitted for women younger than 25 and inadvertently retained for older women. To treat the two age-groups consistently, therefore, we dropped 4,065 intervals of use of reversible contraceptives that were begun in January 1991 or earlier because all such intervals contributed by women under 25 years of age had an unknown duration.

Thus, we analyzed only the 6,867 contraceptive-use intervals contributed by women who either began use for the first time, or who resumed use after discontinuation, between February 1, 1991, and the cutoff date. Therefore, we could not determine proportions continuing use beyond four years. The women who were dropped from the analyses of contraceptive failure and discontinuation because they were using a method in January 1991 were, on average, older than the women we included in these analyses. While excluding the exposure of the women who were dropped does not in theory result in bias (see Appendix), including it would have increased the effective sample size, thereby allowing more precise estimates of probabilities of contraceptive discontinuation and enabling us to analyze discontinuation at longer durations.

*Of all pregnancies with known outcomes preceded by method use that began and ended in our observation period, 16% ended in spontaneous abortion; reported pregnancies resulting from contraceptive failure were no more likely than planned pregnancies to end in spontaneous abortion (15% each). The denominator of the 16% rate is about 9% too small because it is missing 41% of induced abortions, and induced abortions comprise 23% of all pregnancies (see reference 2). If this adjustment is made, then spontaneous abortions reported in the NSFG account for about 15% of the total number of pregnancies estimated to have occurred. The true rate of spontaneous abortion among clinically recognized pregnancies is 12-14% (see reference 6), so it is likely that some induced abortions are reported as spontaneous abortions. If true spontaneous abortions are actually underreported, then reported spontaneous abortions must include induced abortions.

†The questionnaire does not appear to encourage this sort of reporting, nor did the CAPI probes suggest or provide such dates if the respondent was uncertain about the starting and ending dates. It is possible that the sheer length of the interview discouraged probing or caused fatigue-induced memory lapses. The heaping cannot be caused by imputation, as the calendar variables from which the dates were calculated were not imputed.

‡Examination of intervals of pill and of condom use showed no differential in heaping by method. A similar tendency, but much less pronounced (typically 25-30% higher than adjacent months) is apparent in the data from the 1988 NSFG, where method-use records were constructed from dates rather than a calendar. Ironically, one of the claimed advantages of a calendar is that its use reduces heaping of dates.

*Contraceptive Failure, Method-Related Discontinuation and Resumption of Use***Resumption of Use**

For our analysis of the next method used after a contraceptive was discontinued, the duration of prior method use is irrelevant. Therefore, we could expand our sample to include any of the 6,050 women using a method in January 1991 who stopped use during the calendar.

Also, when a woman became pregnant is relevant only for censoring exposure, and matters only for women who were pregnant at interview. We thus cut off observation for pregnant women at 10 months prior to interview (as in the earlier analyses), but continued observation until three months before interview for women who did not report a current pregnancy. (Some women do not report early pregnancies, although they may be aware of them and may not have resumed method use because of them.)

In our analyses of contraceptive failure and discontinuation, we terminated all observations at 10 months before interview. In the analysis of resumption of use, however, the experience of women who discontinued method use during that time could be included. These additional intervals, along with 4,221 intervals from our original sample of 6,867 during the calendar period, yielded a sample of 7,357 for the resumption analysis.

Women's Characteristics

We examined eight potential correlates of contraceptive failure, method-related contraceptive discontinuation and resumption of use after discontinuation of a reversible method—age, parity, race and ethnicity, income, previous method used, desire for a child in the future, work and study status, and marital and cohabiting status.

• **Age.** We created four categories of age at the start of use (younger than 20, 20–24, 25–29 and 30 or older). The oldest age category (30 or older) was not subdivided because of its small sample size. The youngest group includes women who were younger than 15 when they began using a method.

• **Race and ethnicity.** We used the questions about race and Hispanic origin to create a combination variable with the categories non-Hispanic white, non-Hispanic black, Hispanic, and all other.

• **Parity.** We grouped the number of children the respondent had at the time she began using a contraceptive method into

the categories zero, one, and two or more.

• **Income.** We created three categories reflecting income (as a percentage of the federal poverty level) at the time of the interview (no data are available about earlier income)—less than 150%, 150–400% and more than 400%. Roughly half of the women were in the middle category.

• **Previous method.** We did not have a complete method history for the period before the calendar began, which would be necessary to identify with complete accuracy the previous method used. Women who had never used a method can be accurately identified, as all women were asked the first method they ever used and when use of that method began. Women who reported a pregnancy interval that began prior to January 1991 were asked the last method they had used in that interval. For women known to have practiced contraception prior to the period covered by the calendar, we defined the last method used prior to January 1991 as either the first method ever used (for women with no pregnancies prior to the calendar) or the last method used in the pregnancy interval that ended just before the calendar. For second and subsequent methods used in the calendar, we used the method appearing immediately prior in the calendar. We created one variable with four categories: pill, male condom, all other reversible methods and first use of a method.

• **Desire for more children.** Based on a woman's answers to questions about whether she wanted a child in the future at the time each pregnancy occurred and at the time of the interview, we classified each contraceptive-use interval as either a spacing interval (if she wanted to have a child in the future) or a stopping interval.

• **Work and study status.** This variable is a time-varying covariate based on the extensive work history in the survey, along with the education history, which is a little less extensive. Because of lacunae in the five years before interview in which activity could not be determined. There were apparently insufficient variables allocated to contain starting and stopping dates of employment, as there were women who exhausted them well before the interview. Thus, we could not determine what these women were doing after that point. The work history started at age 18; if the woman left school before age 18, there was a gap in her activity history. If a woman was still in school at the interview date (even if she was past high school age and had been out of school for some time before starting again), she was not asked

when she finished high school. This defect applied to all college students. We assumed that women who were still students at the post-high school level had finished high school in June of the year they turned 18. This variable has five categories: in high school, full-time study after high school, full-time work, part-time work or study, and neither studying nor working.

• **Marital and cohabiting status.** This factor is a time-varying covariate based on the marital history and the exhaustive cohabitation history, which included innumerable periods in and out of unions. Women not cohabiting were classified by their formal marital status. This variable has four categories—single (never-married), cohabiting but not married, married and previously married.

Methods

Using the statistical software Stata, we estimated Kaplan-Meier product-limit single-decrement life-table probabilities of contraceptive failure and of discontinuation for method-related reasons. In the analysis of contraceptive failure, we censored women who stopped use for reasons other than failure at the point when they ceased use. In the analysis of method-related discontinuation, women who stopped use for reasons not related to the method were censored at the point when they ceased use. In these analyses, the resulting probabilities indicate what proportion of women would have discontinued use at each duration because of a contraceptive failure or a method-related reason had they not stopped for any other reason.

In contrast, when examining resumption of contraceptive use, we estimated Kaplan-Meier product-limit multiple-decrement life tables.* At each duration following resumption of exposure to the risk of pregnancy, we estimated what proportion of women had started to use the pill, the male condom, sterilization or all other methods combined; the complement is the proportion who were not using a contraceptive method despite being exposed to the risk of pregnancy.

In all instances, we weighted observations with the sample weights from the NSFG, normalized to average 1.0. The number of unweighted observations entering each life table is displayed, along with the 95% confidence intervals. Confidence intervals estimated in Stata for the proportion of women remaining in the analysis at given durations do not reflect the increased uncertainty caused by censoring in intervals between events. This problem is particu-

* We can estimate such models in Stata by creating women who resumed use of any method other than the one being analyzed as exposed to risk forever rather than by censoring them.

larly acute at higher durations, because the confidence interval remains the same after the last observed event, even though fewer and fewer women actually survive to the longest durations because of censoring. We therefore employ the Peto method to produce conservative estimates of 95% confidence intervals.^{11*}

In the analyses of contraceptive failure, method-related discontinuation and resumption of use following discontinuation, we estimated a Cox proportional hazards model separately for each potential correlate to assess whether risks were statistically different across the categories of each factor. The result of each model is an estimate of relative risks—the risk for a particular category relative to the risk for the reference category. For example, in the analyses of method-related discontinuation by age, we estimated risks for age categories relative to the risk at age 20–24.

It is possible that variations in risk across categories of a particular correlate are not causally related to that factor but are observed only because of the confounding effects of other factors. For example, race or ethnicity might appear to have an effect on method-related discontinuation when that factor is examined alone but might not have a significant impact once the effects of income are controlled. It is not feasible, however, to estimate separate life tables for all 23,040 possible combinations of categories for all the factors.

To assess simultaneously the effects of several factors on the risk of contraceptive failure, method-related discontinuation and resumption of use, we used Stata to estimate Cox proportional hazards models. Our goal was to find the simplest models that captured the observed variation in the propensity to experience those outcomes. We started by estimating an initial model with all factors. We next estimated a model that included only the factors with at least one category having a relative risk significantly different from 1.0 at the 5% level. Finally, we combined categories with similar relative risks to produce the simplest model. At each stage, we performed a likelihood ratio test to ensure that the restricted model fit the data as well as the prior unrestricted model.[†]

Observations in these analyses were unweighted, for two reasons: We were examining relative risk factors, not estimating absolute levels of risk; and we wanted to use standard model selection procedures based on likelihood ratio tests.[‡] We employed the same procedure to estimate a final Cox model for resumption of contraceptive use.

Table 1. Percentage of women experiencing contraceptive failure (and 95% confidence interval), by method, according to duration of use, 1995 National Survey of Family Growth

Method	N	Duration of use			
		6 months	12 months	18 months	24 months
Total	6,867	5.5 (4.9–6.3)	8.4 (8.3–10.5)	13.4 (11.8–15.1)	16.7 (14.5–18.2)
Implant	148	0.0 (0.0–0.0)	2.3 (0.6–8.6)	2.3 (0.5–10.5)	2.3 (0.3–16.5)
Injectable	209	1.2 (0.2–6.4)	3.2 (0.6–14.4)	9.3 (2.2–31.8)	9.3 (1.2–45.8)
IUD	59	2.3 (0.3–14.2)	3.7 (0.5–22.6)	9.5 (2.2–32.6)	17.9 (5.5–44.9)
Pill	2,130	3.0 (2.2–4.0)	6.9 (5.5–8.6)	9.5 (7.5–12.0)	12.4 (9.5–15.9)
Diaphragm	166	4.5 (1.8–10.7)	8.1 (3.4–17.9)	11.2 (4.8–24.1)	16.3 (6.9–33.9)
Male condom	2,925	5.4 (4.3–6.6)	8.7 (7.1–10.7)	13.9 (11.3–17.0)	17.6 (13.8–22.2)
Spermicide	164	10.5 (5.3–19.6)	15.3 (7.9–27.7)	22.1 (10.8–40.1)	22.1 (9.1–44.7)
Sponge	111	7.1 (2.4–19.3)	18.4 (8.3–36.0)	27.7 (8.0–62.7)	27.7 (0.03–82.6)
Withdrawal	440	12.5 (8.7–17.6)	18.8 (13.4–25.7)	24.2 (16.9–33.2)	28.5 (18.8–40.7)
Periodic abstinence	250	14.5 (9.8–21.1)	19.8 (13.4–28.4)	27.3 (18.3–38.7)	34.0 (21.7–48.9)
Other	287	32.0 (15.1–55.4)	32.0 (12.2–61.4)	32.0 (12.2–61.4)	32.0 (10.1–66.2)

Finally, we estimated age-specific contraceptive failure rates to produce a total lifetime contraceptive failure rate—the number of contraceptive failures that the typical woman would experience in a lifetime if she used reversible methods of contraception continuously (except for the time spent pregnant after a contraceptive failure) from exact age 15 to exact age 45. This estimate is based on the standard synthetic-cohort assumption—in this case, that the typical woman at each age experiences the average rate of contraceptive failure observed in the NSFG among women of that age.

In this analysis, we included exposure during the calendar period from contraceptive-use intervals that began in or before January 1991 and ended in that month or later. We could do so because we did not need to know the duration of use: The numerator of the age-specific contraceptive failure rate is simply the number of contraceptive failures that occurred among women in that age-group, and the denominator is the number of years of use of a reversible method during the calendar period contributed by women in that age-group (plus the time spent pregnant by women experiencing a contraceptive failure).

If we had based this analysis on only those contraceptive-use intervals that began in or after February 1991, then the age-specific contraceptive failure rates—and hence the total lifetime contraceptive failure rate—would have been biased upward (see Appendix) because the risk of contraceptive failure falls with duration of use and because exposure at long durations of use would be disproportionately omitted (since contraceptive-use intervals that began in or before January 1991 but ended in January 1991 or later would be excluded). We used the same methodology to estimate the total lifetime method-related contraceptive discontinuation rate—the number of times the typical woman would discontinue use of a re-

versible method of contraception for a method-related reason if she used reversible methods of contraception continuously (except for the time spent pregnant following a contraceptive failure) from exact age 15 to exact age 45.

Results

Contraceptive Failure

Table 1 displays probabilities of contraceptive failure for all reversible methods combined and for 11 separate methods: the implant, the injectable, the IUD, the pill, the diaphragm, the male condom, spermicides, the sponge, withdrawal, periodic abstinence[§] and all other methods combined. Overall, 9% of women experi-

*If N_i women are observed at duration i , then at least $N_i = N_i/S_i$ women must have initiated use, where S_i is the life-table probability of surviving to duration i . If exactly N_i women did initiate use, then binomial theory yields the standard error of S_i as $\sqrt{S_i(1-S_i)/N_i}$. The standard error of $Q_i = 1 - S_i$ is therefore $(1 - Q_i)\sqrt{Q_i/N_i}$. This estimate will be conservative if, because of censoring, more than $N_i = N_i/S_i$ women initiated use. To produce 95% confidence intervals for Q_i , we first used the delta method to find the standard error of $\logit(Q_i)$ and then constructed 95% confidence intervals for $\logit(Q_i)$; the antilogits of the upper and lower bounds of the confidence interval for $\logit(Q_i)$ are the upper and lower bounds of the confidence interval for Q_i .

†Performing a test after looking at the results is invalid. We used the tests informally simply to achieve a parsimonious description of the data.

‡The argument for using weights is that they will correct for compositional effects. If all factors that govern the weights are included in the model, there will be no compositional bias. In the NSFG, weights partially reflect the oversampling of blacks and Hispanics. We included race and ethnicity in all models and dropped this variable in the final step only if it did not have a significant effect. The disadvantages of using weights are that estimation is less efficient and that standard model selection strategies based on likelihood ratio tests cannot be employed. The estimates in our final models when weights were used were similar to those when they were not used.

§Of the 250 intervals of use of periodic abstinence, only 33 were intervals of natural family planning, so reliable separate estimates for that method could not be computed.

Contraceptive Failure, Method-Related Discontinuation and Resumption of Use

Table 2. Relative risk of contraceptive failure (and 95% confidence interval), by method and women's characteristics, from Cox proportional hazards models

Method and characteristic	Relative risk	p-value
All reversible methods combined		
Hispanic	1.25 (1.02-1.54)	.034
Low-income	1.54 (1.28-1.85)	.000
High-income	0.89 (0.55-0.86)	.001
First use of any method	0.60 (0.48-0.76)	.000
Full-time study after high school	0.64 (0.44-0.92)	.017
Implant, injectable, pill or IUD	0.46 (0.39-0.55)	.000
Desire for child in future	1.77 (1.46-2.15)	.000
Oral contraceptives		
Age <20	1.55 (1.06-2.27)	.024
Age ≥25	0.58 (0.39-0.87)	.008
Low-income	1.75 (1.26-2.41)	.001
Pill was previous method	2.26 (1.60-3.19)	.000
Male condom		
Hispanic	1.86 (1.37-2.52)	.000
Age ≥25	0.73 (0.56-0.95)	.021
Low-income	1.70 (1.31-2.22)	.000

ence a pregnancy during 12 months of typical use of a reversible contraceptive, and 17% become pregnant during 24 months of typical use. Excluding the residual category of other methods, probabilities of becoming pregnant during the first year of typical use of a method range from a low of 2% for the implant to a high of 20% for periodic abstinence.

Two factors make comparison of efficacy across methods problematic. First, sample sizes for most methods are small. Second, the characteristics of users of different methods, while reflecting the population actually using each method in the United States, vary greatly. For example, 63% of the weighted number of intervals of use of the diaphragm were contributed by women aged 30 or older, compared with only 16% of those of the injectable and 24% of those of the male condom.

Table 2 shows the results of Cox hazards models of contraceptive failure for all reversible methods combined, for the pill and for the male condom. Six factors have a significant impact on the risk of contraceptive failure for all methods combined. The risk of pregnancy is 25% higher among Hispanics than among non-Hispanics; it is 54% higher among low-income women and 31% lower among high-income women than among middle-income women. Moreover, women practicing contraception for the first time are 40% less likely to experience failure than are those who have previously used a contraceptive, and those who are studying full-time after high school are 36% less likely to experience contraceptive failure than are other women. Finally, the risk of pregnancy is 54% lower among those using the implant, the injectable, the pill or the IUD than among those using other reversible methods, and it is 77% higher among those who want to have a child in the future than among those who do not.

Only three factors (two collapsed into only two categories) are predictive of pregnancy during use of oral contraceptives. The risk of contraceptive failure is 55% higher among women younger than 20 and 42% lower among those aged 25 or older than it is among women aged 20-24. Low-income pill users are 75% more likely to become pregnant than are other pill users, and women whose previous method was the pill are more than twice as likely to experience failure as are those whose previous method was not the pill or those who were using the pill for the first time.

The higher risk of contraceptive failure among women whose prior method was the pill is surprising, as we would expect that resumption of a method implies successful prior experience and therefore successful current experience. However, it is possible that prior sporadic or inconsistent pill use not resulting in a contraceptive failure led

to discontinuation and that resumption of sporadic use resulted in method failure.

Finally, Table 2 shows that only three factors are associated with contraceptive failure during use of the male condom. Hispanics have a risk of pregnancy 86% higher than do non-Hispanics, and the risk for low-income women is 70% higher than the risk among other women. Additionally, women aged 25 or older are 27% less likely to experience failure than are women younger than 25.

The total lifetime contraceptive failure rate is 1.8 (not shown); that is, the typical woman who uses reversible methods continuously (except for the time spent pregnant following a contraceptive failure) from age 15 to age 45 will experience 1.8 contraceptive failures. If women using sterilization are included as well, the typical woman will experience 1.3 contraceptive failures from age 15 to age 45.

Discontinuation

Probabilities of discontinuing reversible contraceptive use for a method-related reason are shown in Table 3. The probability of discontinuation within six months is 31%; within 12 months, 44%; and within 24 months, 61%. Excluding the residual category of other methods, probabilities of discontinuing use within six months range from a low of 6% for the implant to a high of 51% for the sponge.

Table 4 displays the results of the Cox hazards model analyses of method-related discontinuation. When all reversible methods are considered together, four factors are predictive of discontinuation. Women aged 30 or older are 28% less likely to stop use than are younger women. Compared with those whose previous method was the pill, women whose previous method was another contraceptive are 15% more likely to discontinue and those who are using a method for the first time are 14% less likely to do so. Women using the implant, the injectable, the pill or the IUD are only 54% as likely to discontinue as those using other reversible methods. Finally, those who want to have a child in the future are 24% more likely to discontinue than those who do not.

Method-related discontinuation of oral contraceptives is significantly associated with only two factors, each collapsed into only two categories. As the table shows, the risk of method-related discontinuation is 28% higher among blacks and women of other races than among whites and Hispanics, and is 39% higher among low-income women than among those with higher incomes.

Table 3. Percentage of women discontinuing contraceptive use for method-related reasons (and 95% confidence interval), by method, according to duration of use

Method	N	Duration of use			
		6 months	12 months	18 months	24 months
Total	6,867	30.6 (29.4-31.8)	43.6 (42.1-45.1)	53.9 (52.2-55.7)	61.3 (59.2-63.4)
Implant	146	6.2 (3.2-11.6)	15.7 (9.9-24.0)	18.3 (11.2-28.4)	20.1 (10.9-34.1)
Pill	2,130	18.0 (16.3-19.8)	32.0 (29.6-34.5)	43.0 (40.0-45.9)	51.3 (47.7-54.8)
IUD	59	18.1 (9.9-30.7)	36.4 (24.0-50.8)	47.8 (31.7-64.4)	59.2 (41.3-75.0)
Diaphragm	166	28.4 (21.5-36.4)	42.8 (33.6-52.6)	53.4 (43.0-63.5)	59.9 (47.3-71.2)
Injectable	209	23.3 (17.2-30.8)	44.4 (34.3-55.1)	54.1 (38.8-68.7)	59.5 (39.0-77.2)
Male condom	2,925	33.9 (31.9-35.9)	47.3 (44.9-49.7)	58.2 (55.4-60.9)	65.8 (62.5-69.1)
Periodic abstinence	250	38.2 (31.9-44.9)	48.8 (41.4-56.3)	60.5 (52.3-68.2)	66.7 (56.0-76.0)
Withdrawal	440	47.4 (42.4-52.5)	57.1 (51.4-62.6)	66.3 (60.3-71.9)	73.4 (66.4-79.3)
Uterine device	164	47.0 (38.7-55.4)	58.2 (48.8-67.1)	65.1 (53.0-75.4)	71.3 (58.3-81.6)
Sponge	111	51.3 (41.1-61.3)	63.7 (51.8-74.1)	85.5 (72.0-93.1)	90.1 (69.3-97.3)
Other	267	89.8 (83.2-94.1)	92.1 (85.0-96.0)	92.1 (85.0-96.0)	92.3 (84.0-96.5)

Table 4. Relative risk of discontinuing contraceptive use for method-related reasons (and 95% confidence interval), by method and women's characteristics, from Cox proportional hazards models

Method and characteristic	Relative risk	p-value
All reversible methods combined		
Age ≥ 30	0.72 (0.66-0.79)	.000
Previous method other than pill	1.15 (1.06-1.24)	.000
First use of any method implant, injectable, pill or IUD	0.86 (0.78-0.96)	.005
Desire for child in future	0.54 (0.50-0.58)	.000
1.24 (1.14-1.35)	.000	
Oral contraceptives		
Black non-Hispanic/other	1.28 (1.10-1.48)	.001
Low-income	1.39 (1.20-1.60)	.000
Male condom		
Black non-Hispanic	0.85 (0.75-0.97)	.014
Age ≥ 25	0.69 (0.61-0.78)	.000
Previous method other than pill or male condom	1.26 (1.09-1.45)	.002
First use of any method	0.77 (0.67-0.88)	.000
Never-married/ previously married	1.21 (1.07-1.38)	.003

Four factors are predictive of discontinuation of the male condom. Black non-Hispanic women are 15% less likely to stop using the male condom than are other women, and women aged 25 or older are 31% less likely to discontinue than are younger women. Compared with women whose prior contraceptive was the pill or the male condom, those whose previous method was another contraceptive are 26% more likely to discontinue and women who are using a contraceptive method for the first time are 23% less likely to discontinue. The risk of discontinuation is 21% higher among single or previously married women than among married or cohabiting women.

The total lifetime method-related contraceptive discontinuation rate is 9.5; that is, the typical woman who uses reversible methods of contraception continuously (except for the time spent pregnant following a contraceptive failure) from age 15 to age 45 will discontinue use for a method-related reason 9.5 times. If women using sterilization are included as well, the typical woman will discontinue use of contraception for a method-related reason 7.2 times from age 15 to age 45.

Resumption of Use

Probabilities of starting use of the pill, sterilization, the male condom and all other methods following discontinuation of a reversible method are shown in Table 5. Within one month after discontinuing a method, 68% of women are practicing contraception—17% are relying on the pill,

5% on vasectomy or tubal sterilization, 25% on the male condom and 20% on other methods. The proportion resuming use after becoming exposed to the risk of pregnancy increases to 76% by three months, 79% by six months and 82% by 12 months.

There is not much variation among women according to most characteristics (not shown). Proportions starting use within three months of becoming exposed range from 74% among women aged 30 or older to 78% among women aged 25-29, from 70% among blacks to 78% among whites, and from 74% among low-income women to 78% among high-income women. A detailed examination of differences by previous method shows that at three months, the proportion resuming method use ranges from 73% of women who discontinue pill use to 79% among those who stop relying on withdrawal. Those who discontinue pill use are more likely to switch to the male condom than to resume using the pill (30% vs. 18%). In contrast, those who discontinue use of the male condom are more likely to resume use of this method than to switch to the pill (30% vs. 22%). Not surprisingly, switching to sterilization from a reversible method increases with age (not shown). This pattern is more common among whites than among blacks or Hispanics, and is more frequent among women who discontinue a contraceptive other than the pill, the male condom or withdrawal than among women who stop using those methods.

Results of a Cox proportional-hazards model (Table 6, page 70) show that whites are 12% more likely to resume use than are non-whites. Compared with women aged 20-29, women younger than 20 are 7% more likely to resume use and those aged 30 or older are 14% less likely. Women with two or more children are 17% more likely to resume use than are primiparous or nulliparous women. The rate of resumption of use is 7% lower among low-income women and 8% higher among high-in-

come women than among middle-income women.

Those whose prior method was the pill are 6% less likely to resume use than are those whose prior contraceptive was another method. Compared with women who are working full-time or working and studying part-time or are in high school, those who are studying full-time following high school are 15% more likely to resume use, and those who are neither studying nor working are 6% less likely to do so. The likelihood of resuming use is 5% lower for women who want to have a child in the future than for those who do not. Finally, women whose last interval of method use ended in a contraceptive failure are 31% more likely to resume use than are those who discontinued use for any other reason.

Discussion

Estimates of the percentage of women experiencing a pregnancy during the first year of typical use (Table 7, page 70) were previously developed by the first author and were adopted by the U.S. Food and Drug Administration (FDA).¹² Compared with these estimates, the rates presented in Table 1 are much higher for the implant, the injectable and the IUD, and are slightly higher for the pill. In contrast, they are much lower for the diaphragm, the male

Table 5. Percentage of women resuming use of contraceptives after discontinuation, by duration of use (in months), according to method discontinued and subsequent method used

Discontinued method and duration	All	Subsequent method			
		Pill	Sterilization	Male condom	Other
All (N=7,357)					
1	68.1 (67.5-68.7)	17.3	5.4	25.0	20.3
3	75.9 (74.8-77.0)	19.3	5.8	28.9	21.9
6	79.2 (77.9-80.4)	20.4	6.0	30.2	22.8
12	82.0 (80.5-83.4)	21.1	6.1	31.5	23.3
Pill (N=2,568)					
1	65.4 (64.3-66.5)	14.6	5.6	28.0	17.2
3	73.1 (71.1-75.0)	18.4	6.0	30.2	18.6
6	76.2 (73.9-78.3)	20.0	6.2	31.1	19.0
12	79.2 (76.6-81.6)	21.2	6.3	32.1	19.6
Male condom (N=3,046)					
1	67.9 (66.9-68.8)	21.2	4.6	24.0	18.1
3	76.6 (74.8-78.2)	22.4	4.9	30.2	19.1
6	79.8 (77.8-81.7)	23.2	5.1	32.1	19.5
12	82.9 (80.5-85.0)	23.7	5.1	34.1	20.0
Withdrawal (N=443)					
1	72.4 (70.2-74.6)	14.8	2.5	28.5	26.6
3	79.2 (74.1-83.5)	15.3	2.6	32.0	29.3
6	84.7 (78.7-89.3)	15.8	3.0	33.5	32.3
12	86.7 (79.1-91.9)	16.4	3.1	33.9	33.3
Other (N=1,300)					
1	72.1 (70.8-73.4)	14.3	8.1	20.3	29.4
3	78.9 (76.2-81.3)	15.3	8.4	22.4	32.7
6	81.9 (79.1-84.5)	15.8	8.6	23.3	34.2
12	84.0 (80.6-86.8)	16.5	8.7	24.1	34.7

Contraceptive Failure, Method-Related Discontinuation and Resumption of Use

Table 6. Relative risk of resuming contraceptive use after discontinuation (and 95% confidence interval), by women's characteristics, from Cox proportional hazards models

Characteristic	Relative risk	p-value
White	1.12 (1.08-1.16)	.000
Age <20	1.07 (1.03-1.12)	.001
Age ≥20	0.86 (0.83-0.90)	.000
Parity ≥2	1.17 (1.12-1.22)	.000
Low-income	0.93 (0.90-0.97)	.001
High-income	1.08 (1.04-1.12)	.000
Previous method was pill	0.94 (0.91-0.97)	.000
Full-time study after high school	1.15 (1.10-1.21)	.000
Not working/studying	0.94 (0.90-0.98)	.007
Desire for child in future	0.95 (0.91-0.98)	.005
Previous use ended in failure	1.31 (1.27-1.36)	.000

condom, spermicides and the sponge,* somewhat lower for periodic abstinence and about the same for withdrawal.

These differences may result, in large part, from differences in the source of the data and in the numbers of women involved. The estimates in Table 7 for the implant, the injectable, the IUD and the sponge are based on large prospective clinical trials; the estimates for these methods shown in Table 1 are based on much smaller numbers (ranging from 59 for the IUD to 209 for the injectable) from retrospective reports. For spermicides, periodic abstinence, the diaphragm, the male condom and the pill, the estimates in Table 7 are derived from the experience of married women in the 1976 and 1982 rounds of the NSFG and from that of all women participating in the 1988 NSFG.²³

However, the estimates from the prior NSFGs (in Table 7) and those from the 1995 NSFG (in Table 1) differ in two important ways. First, the results from the prior NSFGs were standardized to reflect the estimated probabilities of pregnancy that would be observed if users of each method had the same characteristics (the same age distribution, the same proportion seeking to prevent further child-bearing instead of delaying the next wanted pregnancy, the same parity distribution and the same proportion living in poverty); the data from the 1995 NSFG, in contrast, are not standardized in this way. Sec-

*About half (49%) of the weighted number of intervals for the sponge in Table 1 are contributed by nulliparous women. The first-year probability of pregnancy in Table 1 is similar to the estimate in Table 7 for nulliparous women (20%), but is far lower than the estimate for parous women (40%).

the three IUDs listed in Table 7, the LNG IUD is not available in the United States and the Progesterone-T is not commonly used. Therefore, we discuss here only results for the Copper-T IUD.

ond, the results from the 1988 NSFG were adjusted for estimated underreporting of abortion. For spermicides, periodic abstinence, the diaphragm, the male condom and the pill, estimates from the 1988 NSFG that were neither standardized nor adjusted for abortion underreporting¹⁴ are similar to those shown in Table 1.

Compared with previous estimates of method-related discontinuation during the first year of use developed by the first author and adopted by the FDA (Table 7),¹⁵ the estimates based on the 1995 NSFG (Table 3) are about the same for the pill, the diaphragm and spermicides. However, the current estimates are four percentage points higher for the implant; eight percentage points higher for the male condom; and 12-14 percentage points higher for the injectable, the sponge, periodic abstinence and the IUD.[†] As with failure rates, the two sets of discontinuation rates are not comparable, because the estimates adopted by the FDA for the implant, the injectable and the IUD are based on results from large prospective clinical trials, whereas those presented in Table 3 are based on small numbers of retrospectively reported intervals of use. Another difficulty is that methods were not classified by brand in the NSFG's monthly calendar of contraceptive use. A change from one brand or type of pill or male condom to another could not, therefore, be detected. In contrast, in a clinical trial of a particular brand of oral contraceptive, a switch from that brand to another brand would be considered a method-related reason.

The one-year discontinuation rate for the injectable that was adopted by the FDA and is shown in Table 7 was calculated from the results of two World Health Organization (WHO) trials of the 150-mg dose injected every 90 days.¹⁶ It is considerably lower than the rates

of discontinuation reported in four U.S. studies (50-77%),¹⁷ all of which were conducted after the drug had been approved by the FDA. The results from these six studies are not strictly comparable, because discontinuation for reasons such as desiring to become pregnant and no longer having intercourse was included in the four U.S. studies. Nevertheless, the proportions continuing use would still be far lower than the estimates used by the FDA if discontinuation for reasons unrelated to use of the injectable were excluded.

Note that discontinuation among users of the injectable has been measured differently from discontinuation among users of other methods in clinical trials. As in the NSFG, a woman in a clinical trial is usually considered to be a user of a method as long as she considers herself to be using that method. However, in clinical studies of the injectable, a woman is considered to have discontinued use if she does not re-

Table 7. Percentage of U.S. women experiencing an unintended pregnancy during the first year of typical use and the first year of perfect use of contraceptives, and the percentage who have discontinued use by the end of the first year, by method

Method	% experiencing failure during		% discontinuing*
	Typical use†	Perfect use‡	
Chance§	85	85	na
Spermicides**	26	6	80
Periodic abstinence	25	u	37
Calendar	u	9	u
Ovulation method	u	3	u
Symptothermal††	u	2	u
Postovulation	u	1	u
Cervical cap‡‡			
Parous women	40	26	58
Nulliparous women	20	9	44
Sponge			
Parous women	40	20	58
Nulliparous women	20	9	44
Diaphragm‡‡	20	6	44
Withdrawal	19	4	u
Condom§§			
Female	21	5	44
Male	14	3	39
Pill	5	u	29
Progesterin only	u	0.5	u
Combined	u	0.1	u
IUD			
Progesterone T	2.0	1.5	19
Copper T 380A	0.8	0.6	22
LNg 20	0.1	0.1	19
Injectable	0.3	0.3	30
Implant	0.05	0.05	12
Tubal sterilization	0.5	0.5	0
Vasectomy	0.15	0.10	0

*Among couples attempting to avoid pregnancy, the percentage who discontinue use within one year. †Among typical couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. ‡Among couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. §The percentages becoming pregnant are based on data from populations in which contraception is not practiced and from women who cease using contraceptives to become pregnant. In such populations, about 89% become pregnant within one year. This estimate was reduced slightly to represent the percentage who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraceptive use altogether. **Foams, creams, gels, vaginal suppositories and vaginal film. ††Cervical mucus (ovulation) method supplemented by calendar in the preovulatory phase and by basal body temperature in the postovulatory phase. ‡‡With spermicidal cream or jelly. §§Without spermicides. Notes: na=not applicable. u=unavailable. Source: See reference 6.

turn for her next shot within 14 weeks (15 weeks in some studies), even though contraceptive protection probably extends well beyond that period, and even if she returns thereafter and receives another injection. This convention of classifying such women as discontinuing but not pregnant at 14 (or 15) weeks leads to an overestimate of the discontinuation rate¹⁸ and to an underestimate of the pregnancy rate if women miss an injection and become pregnant after 14 weeks but still consider themselves to be using the injectable.

In contrast to the 1995 NSFG estimates, the first-year discontinuation rates shown in Table 7 for spermicides, periodic abstinence, the diaphragm, the male condom and the pill were computed in two steps. In the first step, the proportions of married women in the 1982 NSFG who discontinued use were calculated under the assumption that the only forms of discontinuation were method change and complete termination of contraceptive use while still at risk of an unintended pregnancy.^{19*} These discontinuation rates were then standardized to reflect the estimated probabilities of continuation that would be observed if users of each method had the same characteristics (the same distribution by age, race and education). In the second step, we multiplied the complement of the discontinuation rates (which do not take pregnancy into consideration) obtained in the first step by the complement of the first-year typical-use failure rate in the second column of Table 7 to obtain the probability of continuing use among those seeking to avoid pregnancy.

Conclusion

The risk of failure during typical use of reversible contraceptives in the United States is not low—overall, 9% of women

*To obtain the estimate for the sponge, which was not approved for use in the United States until 1983, we substituted the probability of discontinuation (excluding pregnancy) for the diaphragm in the first step.

†We did not use the standard NCHS hierarchy, because its ranking of methods does not reflect current understanding of relative contraceptive efficacy (see reference 8). The NCHS orders methods, from most to least effective method during typical use, as follows: female sterilization, male sterilization, the implant, the injectable, oral contraceptives, emergency contraceptive pills, the IUD, the diaphragm, the male condom, the female condom, spermicidal foam, the cervical cap, the sponge, the spermicidal suppository, spermicidal jelly or cream, periodic abstinence, withdrawal and other methods. Our hierarchy recognizes that emergency contraceptive pills not an ongoing method of contraception, that the IUD is far more effective than the pill or the injectable, that the male condom is more effective than the diaphragm and that there is no evidence that one type of spermicide is more effective than another.

become pregnant within one year of starting use. The typical woman who uses reversible methods of contraception continuously from her 15th to her 45th birthday will experience 1.8 contraceptive failures. Contraceptive failure rates computed from the 1995 NSFG are similar to those computed from the 1988 NSFG²⁰ for the five methods that can be compared: pill (7% in the 1995 NSFG vs. 5% in the 1988 NSFG), male condom (9% vs. 7%), diaphragm (8% vs. 10%), periodic abstinence (20% vs. 21%), and spermicides (15% vs. 13%). These high pregnancy rates do not reflect the inherent efficacy of methods when used correctly and consistently (see Table 7),²¹ but instead reflect imperfect use (because most reversible methods are difficult to use correctly).

Discontinuation of use of a reversible contraceptive for a method-related reason is very common—31% of women stop within six months of starting use, and 44% do so within 12 months. The typical woman who uses reversible methods of contraception continuously from her 15th to her 45th birthday will discontinue contraceptive use for a method-related reason nearly 10 times. Such high rates of discontinuation almost surely reflect dissatisfaction with current methods. Fortunately, the vast majority of women resume use of contraceptives shortly after becoming exposed to the risk of pregnancy.

Multivariate analyses identified several subgroups consistently at risk of adverse outcomes. Low-income women have a much higher risk of contraceptive failure than other women for all reversible methods combined, for oral contraceptives and for the male condom, and a lower likelihood of resuming contraceptive use after discontinuing a reversible method. Hispanics have a higher risk of contraceptive failure for all reversible methods of contraception combined and for the male condom. Black non-Hispanic women have a higher risk than other women of discontinuing use of oral contraceptives and of the male condom for a method-related reason. Women who want a child in the future have higher risks of contraceptive failure and discontinuation for a method-related reason. Of special interest for public policy are the increased risk of contraceptive failure among the poor and the decreased likelihood of resuming use after discontinuation of a reversible method among the poor and among women of color.

Our analyses suffer from the inherent limitations of self-reported data. It is likely both that sensitive behaviors and

events—such as induced abortion—are not completely reported in the NSFG and that other information—such as precisely which methods were used in each month since January 1991—simply cannot be accurately recalled. Moreover, the concept of use is an elastic one that depends entirely on whether a woman considers herself to be a user of a particular method at a specific point in time. Finally, women were not asked in the NSFG why they stopped using a method; instead, the reason must be inferred from other information they gave. The degree to which the picture we paint more or less accurately reflects reality is, therefore, unknowable.

Appendix

Contraceptive Overreporting

The 12-month probability of pregnancy during use of the IUD is 3.7% (see Table 1); using the estimated standard error of this estimate, we find that the chance of observing a risk that high is only 6.3% if the true probability is 0.8%, the estimated probability of pregnancy during typical use of the Copper-T IUD based on results from large U.S. clinical trials.²² Likewise, the 12-month probability of pregnancy during use of Norplant is 2.3%; the chance of observing a risk that high is only 1.3% if the true probability is 0.5%, the estimated probability of pregnancy during typical use of Norplant based on results from large U.S. clinical trials.²³ The joint chance of observing risks that high for both methods is only 0.08% if the true probabilities are 0.8% and 0.5%, respectively. These results are suggestive of overreporting of acknowledged pregnancies as contraceptive failures in the NSFG.

Discontinuation and Resumption

As a first step, we assumed that use of a method began when the code for that method appeared as one of the methods in a month in the focal period and ended when we found a subsequent month in which the code did not appear. Such a classification scheme would result in multiple spells of use for women who used more than one method in a month. To avoid this result, we generally classified multiple method use in each month by the following hierarchy based on efficacy: male or female sterilization, the implant, the injectable, the IUD, oral contraceptives, the male condom and a residual group of all other methods.[†] The reason for stopping was not indicated in the calendar but could usually be determined or imputed by cross-checking other variables for the woman, either in the main respondent file or in the related pregnancy interval file:

- If the woman was using a method during the month in which she became pregnant, the NSFG interviewer asked whether she had stopped practicing contraception before she became pregnant. If the woman had not stopped use, we deduced that the pregnancy resulted from contraceptive failure. The NSFG interviewer also asked which method or methods she was using when the pregnancy occurred, but we did not always find these methods recorded in the calendar. In some cases, the method reported was used along with another method, and we classified these cases according to our efficacy hierarchy. There were also some cases in which both vasectomy and a reversible method were being used, in which case we clas-

sified the method for that segment as sterilization (although it is possible that the woman had more than one partner). In case of ambiguity, we relied on the method calendar, as we needed it to calculate dates and had fewer problems if we used a consistent source for other data.

• There are two variables for date of conception in the pregnancy interval file. One, CONCEPT, is the date computed by the CAPI program based on the date of pregnancy termination and the gestational length in weeks or months (with probes for unknown values). The other variable, DATECON, ostensibly based on the same questions, with all missing values imputed, is a recode by the National Center for Health Statistics (NCHS). There is no documentation of the formula used to calculate CONCEPT, which differs from DATECON in about 30% of the cases. Most of the differences are of only one month in either direction, and in all of these cases DATECON appears more (or at least equally) reasonable. CONCEPT has a few clearly wrong values in addition to the unknown values. (One is a date that would fall in an earlier pregnancy interval; two others imply gestational lengths of more than 10 months.) For this reason, we preferred to use DATECON. Unfortunately, however, we had to rely on CONCEPT to answer questions about whether method use was stopped.

In every case, we used DATECON to determine length of use. We relied on CONCEPT only to determine if there was an answer to the questions about stopping use. Where CONCEPT differed from DATECON, we assumed that the answer to the questions should be based on DATECON. For instance, if a woman stopped using contraception in May, and CONCEPT had a value equivalent to May, the woman was asked if she had stopped use before she became pregnant. If she said "no," we assumed there was a contraceptive failure in the month of DATECON, even if DATECON was April or June rather than May. We further assumed that method use stopped in the month of DATECON, adding or subtracting a month from the duration of use if necessary to make the duration conform to DATECON. If there was more than a month's difference, we did not make this adjustment. There are very few such cases, and even fewer in which a method was used in one or both months (CONCEPT or DATECON). In these few cases, we assumed there was a failure if method use continued for at least one month after DATECON; otherwise, we assumed the outcome was unknown.

• If a woman reported method use continuing after the beginning of the pregnancy, she was not asked whether she had stopped using the method. Most of these cases were probably true contraceptive failures, but some, especially those in which use continued throughout the pregnancy, appear to represent either noncontraceptive use (e.g., condom use for prevention of sexually transmitted infections), or perhaps a misunderstanding of the meaning of "stopped use." If the pregnancy lasted longer than five months and the woman practiced contraception throughout its duration, we assumed that the conception resulted from contraceptive failure if it was either unwanted or mistimed.

• If a woman had stopped practicing contraception before she became pregnant, the NSFG interviewer asked a series of questions about whether the pregnancy was planned. We used the answers to determine whether the last method the woman used prior to the pregnancy was stopped because the woman planned to get pregnant. This deter-

mination also required matching data between the two files, with the attendant complications.

• For pregnancy intervals that began before 1991 but ended during the calendar period, women were not asked the detailed set of questions regarding method use at the time of conception, which we used to determine contraceptive failure. We based the assessment of failure on whether method use was stopped before the pregnancy began; if it was not, we assumed the method used at the time of conception was the method found in the calendar on the calculated conception date.

• The contraceptive use calendar for the 1995 NSFG has more than 16 separate variables for each month of the observation period, allowing the listing of complex combinations of methods. Some respondents appear to alternate methods, rotating from one to another within a single month in a repeating pattern. For example, one woman reported using sponge and rhythm, condom and rhythm, and foam and rhythm separately in each month. There is no way to determine the order in which these methods were used. However, if a woman used exactly two methods, she was asked whether the methods were used simultaneously or sequentially. If she used three or more methods, she was asked the various ways in which they were combined. If there was only one combination, and it included all methods used in the month, we assumed that use was simultaneous; otherwise, we assumed the methods were used sequentially. We have used the following rules for dealing with these combinations:

1. If two methods were used sequentially in one month, and one was used in the previous month, while the other was used in the following month, we treated the case as a method change in the month in which both were found.
2. If multiple methods, none of which ranked higher than the male condom in effectiveness, were used sequentially, we included them in the residual category "other methods."
3. Sequential use of multiple methods, at least one of which ranked higher than the male condom in effectiveness, seems implausible (with the possible exception of vasectomy used with one partner and another method used with another partner). In the analyses, we included these cases in the residual category "other methods."
4. If more than one method was used simultaneously, at least one of which was ranked more effective than male condom, we used the code of the most effective method.
5. If two or more methods, the most effective of which was the male condom, were used simultaneously, we included them with male condoms.
6. If two or more methods were used simultaneously, all of which were less effective than the male condom, we included them with the residual category "other methods."

• Examination of the dates of union and dates when the woman was not having intercourse, as well as the dates of menopause and noncontraceptive sterilization, revealed if a woman was no longer exposed to risk when she stopped use. We assumed that if use ended in one month and a woman reported not having intercourse in either that month or the following month, then she was not at risk when she discontinued use of her method.

• The appearance of different methods of contraception in two consecutive months indicated that the woman had changed methods.

• We classified other discontinuation with no immediate change to another method, in a period when the woman reported she was having inter-

course and was not sterile, as "stopped, other." This category includes stopping use in the month a pregnancy occurred, if the pregnancy was not planned and was not a contraceptive failure.

Some data were missing for reasons that are unclear. According to the Round 5 user's guide, a pair of errors in the skip patterns caused about 5% of the pregnancy intervals to have missing data for a series of questions including wantedness of the pregnancy, and also for such questions as whether method use was stopped before conception. (The answer to this latter question is important for our purposes, as there is no other way to distinguish a contraceptive failure from a very short period of nonuse preceding the pregnancy.) The more damaging of these errors, according to the user's guide, is that women who did not explicitly answer yes when asked if they had ever had voluntary intercourse were not asked questions about contraception and timing. However, as more than 95% of the women interviewed were not even asked whether they had ever had voluntary sex (either because they had never had sex, or because their first act of intercourse was voluntary) and therefore could not have given an affirmative answer, this explanation cannot be correct.

We assumed that a woman became potentially exposed to the risk of resuming contraceptive use in three situations:

1. She had a contraceptive failure, in which case she became potentially exposed when the ensuing pregnancy ended.
2. She stopped practicing contraception because she wanted to become pregnant, in which case she became potentially exposed after that pregnancy ended.
3. She discontinued use for some other reason, in which case she became potentially exposed immediately.

If, in the month she became potentially exposed to risk, she started using a method, we classified her as actually exposed to risk and as resuming use. If, on the other hand, she did not resume contraceptive use, we checked to see whether she reported not having intercourse in that month or whether she was trying to get pregnant. If she reported that she was not having intercourse or was trying to become pregnant, we classified her as not being at risk of pregnancy and as being potentially exposed to the risk of resuming use in the next month, and the algorithm was applied again. We then calculated the life-table probability of beginning use of another method (including another period of use of the same method).

Possible Bias due to Interval Selection

• Lack of bias is dependent on being in a steady state, a condition unlikely to be met as methods wax and wane in popularity. To test the assumption that including only contraceptive-use intervals that began in or after February 1991 does not result in bias, we examined only those intervals contributed by women aged 25 or older at interview. Among the 4,045 intervals that began in February 1991 or later, the 36-month probabilities of contraceptive failure and method-related discontinuation were 20% and 71%, respectively. Including not only those 4,045 intervals but also the 1,586 intervals that began before February 1991 and ended in February 1991 or after, the 36-month probabilities of contraceptive failure and method-related discontinuation were 18% and 64%, respectively.

The difference between the two estimates is only partly due to differences in the characteristics of

(continued on page 93)

reference 3); Stevens-Simon C, Kelly LS and Singer D, 1996, op. cit. (see reference 2); Stevens-Simon C et al., 1997, op. cit. (see reference 4); Brown SS and Eisenberg L, 1995, op. cit. (see reference 3); and Maynard R and Rangarajan A, Contraceptive use and repeat pregnancies among welfare-dependent teenage mothers, *Family Planning Perspectives*, 1994, 26(5):198-205.

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Failure, Discontinuation...

(continued from page 72)

the women who were already practicing contraception in 1991, as opposed to those who began using a method later. Many women misreported their starting dates of method use to be in January of each of the calendar years. If we consider all use that began in January 1991 or later, the 36-month probabilities of contraceptive failure and method-related discontinuation are 18% and 68%, respectively. These lie between the estimates derived from all use and those derived from use beginning in February 1991 or later.

Moreover, the differences in results based on intervals starting in or after January 1991 and results based on intervals starting in or after February 1991 are of similar magnitude to the differences in results based on intervals starting in or after January 1991 and results based on all intervals. Therefore any bias caused by selecting only intervals that began in or after February 1991 is probably dwarfed by bias due to reporting error.

When Cox regression models of contraceptive failure and method-related discontinuation with the same factors in the top panels of Tables 2 and 4 were run on all contraceptive-use intervals and on intervals that began in January 1991 or after, the qualitative conclusions are identical, and the quantitative results are similar. The difference in estimated coefficients is at most 1.1 times the size of the standard error of the coefficient in the model based on all intervals and is generally much smaller; the difference averages 40% of the standard error in the contraceptive failure model and 66% of the standard error in the model of method-related discontinuation.

*The total lifetime contraceptive failure rate when exposure and contraceptive failures from all contraceptive-use intervals that began in or before January 1991 but ended in that month or later are included is 1.8. In contrast, if only those intervals that began in February 1991 or thereafter are included, the total lifetime contraceptive failure rate would be 2.7.

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BRIEF REPORT

Natural Limits of Pregnancy Testing in Relation to the Expected Menstrual Period

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THE PRACTICAL REFERENCE POINT for the detection of pregnancy is the first day of a woman's missed period, ie, the day on which she expects her next period to begin. Unless a woman carries out special tests for ovulation, her only basis for predicting the onset of her next menses is her usual cycle length. Most women are able to report their usual cycle length, despite the natural variability from cycle to cycle. This variability in cycle length is due largely to variation in the number of days from the beginning of menses to ovulation.¹

There is no practical way to identify conception before implantation of the blastocyst. The time of implantation has its own natural variability, ranging from 6 to 12 days after ovulation.² Thus, the exact interval from onset of previous menstrual period to ovulation and then to the detectability of a pregnancy is inherently difficult to predict.

The trophoblast cells of the conceptus produce human chorionic gonadotropin (hCG) in amounts that increase exponentially following implantation. This production of hCG provides the basis for all pregnancy tests, including home test kits. In 1999, about 19 million over-the-counter pregnancy test kits were sold in the United States, with sales of about \$230 million.³ Kits typically instruct women to test for pregnancy "as

See also Patient Page.

Context Pregnancy test kits routinely recommend testing "as early as the first day of the missed period." However, a pregnancy cannot be detected before the blastocyst implants. Due to natural variability in the timing of ovulation, implantation does not necessarily occur before the expected onset of next menses.

Objective To estimate the maximum screening sensitivity of pregnancy tests when used on the first day of the expected period, taking into account the natural variability of ovulation and implantation.

Design and Setting Community-based prospective cohort study conducted in North Carolina between 1982 and 1986.

Participants Two hundred twenty-one healthy women 21 to 42 years of age who were planning to conceive.

Main Outcome Measures Day of implantation, defined by the serial assay of first morning urine samples using an extremely sensitive immunoradiometric assay for human chorionic gonadotropin (hCG), relative to the first day of the missed period, defined as the day on which women expected their next menses to begin, based on self-reported usual cycle length.

Results Data were available for 136 clinical pregnancies conceived during the study, 14 (10%) of which had not yet implanted by the first day of the missed period. The highest possible screening sensitivity for an hCG-based pregnancy test therefore is estimated to be 90% (95% confidence interval [CI], 84%-94%) on the first day of the missed period. By 1 week after the first day of the missed period, the highest possible screening sensitivity is estimated to be 97% (95% CI, 94%-99%).

Conclusions In this study, using an extremely sensitive assay for hCG, 10% of clinical pregnancies were undetectable on the first day of missed menses. In practice, an even larger percentage of clinical pregnancies may be undetected by current test kits on this day, given their reported assay properties and other practical limitations.

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early as the first day of the missed period." To evaluate the number of pregnancies detectable at the missed period, we estimated the day of implantation relative to the expected first day of the missed period among a group of women with naturally conceived pregnancies.

METHODS

We studied 221 healthy North Carolina women who were planning to become pregnant.⁴ Women with no known fertility problems were recruited in 1982-1986 from the local community and enrolled at the time

they discontinued their method of birth control. Women ranged from 21 to 42 years of age; mean age was 30 years, with 5% older than 35 years. Most were college educated, and 96% were white; further details are provided elsewhere.⁴ All participants provided informed consent, and the study was ap-

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PREGNANCY TESTING AND EXPECTED MENSTRUAL PERIOD

Table. Estimated Day of Implantation of Clinical Pregnancies Relative to the Expected Onset of the Next Menstrual Period

Estimated Day of Implantation Relative to First Day of the Expected Period	Estimated No. of Conceptions on This Day	Cumulative %
-7 and earlier	55	40
-6	15	51
-5	14	62
-4	9	68
-3	7	74
-2	8	79
-1	8	85
Day of expected period	6	90
+1	1	90
+2	3	93
+3	3	95
+4	2	96
+5	1	97
+6	0	97
+7	0	97
+8	1	98
+9	0	98
+10	1	99
+11 and later	2	100
Total	136	

proved by the National Institute of Environmental Health Sciences institutional review board. Women kept menstrual diaries and froze daily urine specimens for later analysis. During the study, 151 women conceived a clinical pregnancy (defined as a pregnancy lasting 6 weeks beyond the last menstrual period).

Urine samples were assayed for hCG with an extremely sensitive immunoradiometric assay.³ Detection limit was 0.01 ng of hCG per milliliter, which is approximately 0.13 mIU/mL.⁴ This assay was directed primarily at intact hCG, but also cross-reacted with the free-beta subunit of hCG. The hCG produced by clinical pregnancy was easily distinguished from background levels by its pattern of exponential rise. We defined the onset of pregnancy-related hCG as the earliest day of sustained hCG elevation in which hCG concentration exceeded 0.015 ng/mL. We regard this as the best available marker of implantation.²

Among the 151 clinical pregnancies, we were unable to determine the onset of hCG for 9 (in most cases because crucial urine samples were missing). Of the remaining 142 preg-

nant women, 136 provided information about their "usual cycle length." These 136 women provided the basis for the current analysis. The median reported cycle length was 29 days, with 96% of women reporting lengths between 23 and 35 days (range, 19-60 days). We previously tested the validity of self-reported cycle length by comparing it with the observed length of the woman's follicular phase during the study. The correlation was 0.55.⁶

Ninety-four of the eligible 136 women reported their usual cycle length as a single number. We used this usual cycle length to estimate the day on which a woman would expect her next period (eg, a woman with a usual cycle length of 28 days would expect her period on day 29.) For women who conceive, the day on which the next period is expected is the "first day of the missed period." The remaining 42 women reported their usual cycle length as a range (eg, "28-30 days"). For these women, we used the upper limit of the range to determine the first day of the missed period.

RESULTS

The TABLE shows the estimated day of implantation relative to the first day of the missed period. Implantation occurred by the first day of the missed period in 90% of pregnancies (95% confidence interval [CI], 84%-94%). By 7 days after the first day of the missed period, 97% of all clinical pregnancies had implanted (95% CI, 94%-99%). After excluding the 21 women who reported that their cycles were "irregular," results were unchanged (90% and 97%).

COMMENT

Implantation can occur surprisingly late in relation to a woman's expected menses. For 10% of clinical pregnancies in our study, implantation occurred after the first day of the next expected period. This represents an insurmountable limitation of hCG-based pregnancy testing on the first day of the missed period. A perfectly sensitive assay for hCG could not have detected 100% of these clinical preg-

nancies even 10 days after the period was expected (Table).

These data describe the physiologic limits of early pregnancy testing. However, we did not directly test the performance of home test kits. The performance of a single, qualitative assay in the hands of a layperson depends on many factors. One factor is the assay detection limit. While detection limits are not routinely provided with test kits, a Web site lists assay detection limits for 40 commercial kits as determined by telephoning the manufacturers.⁷ These reported assay detection limits of hCG range from 15 to 100 mIU/mL, with most kits between 25 and 50 mIU/mL. Detection limits for some kits may be slightly more sensitive than reported by manufacturers.⁸ Even so, an assay detection limit of 15 mIU/mL is about 100 times less sensitive than the assay we used to define implantation (0.13 mIU/mL). This implies that most current test kits would not reliably detect hCG on the day of implantation. Chard⁹ estimates that an assay with a detection limit of 25 mIU/mL will begin to detect pregnancy around 3 or 4 days after implantation.

Other factors also affect the performance of test kits. Urinary dilution may reduce detection limits.¹⁰ Not all test kits measure the same components of hCG; some measure only intact hCG, while others measure intact plus the free beta.^{11,12} The ratio of these hCG components may vary from pregnancy to pregnancy,¹¹ which could affect the detection limits of specific tests. In addition, user errors have been reported to contribute to false-negative findings.¹³

The instruction to test on the "first day of the missed period" may not mean the same thing to all women. Women do not know their period is late until the second day of their expected period. If women think the first day of their missed period is after they know their period is late, the percent of false-negative test results would decrease slightly.

How all these factors affect actual test kit performance is hard to predict. If kits do reliably detect pregnancy by the third

implantation, then about one fourth of clinical pregnancies would produce a false-negative test result on the first day of the missed period. Previous studies do not provide information on this point because they lacked proper attention to the timing of the test in relation to expected menses.¹³

It should not necessarily be the goal of home test kits to achieve the lowest possible limits of hCG detection. About one fourth of all pregnancies detectable at implantation fail very early.⁴ The detection of these events by highly sensitive home test kits would be of uncertain benefit to women.

The interpretation of a negative pregnancy test result on the first day of the missed period deserves comment. Some package inserts state that if a test is nega-

tive, "you are probably not pregnant." One says "you are NOT PREGNANT" (emphasis in the original). This unfounded assurance could have important consequences. For example, women with a negative test result may fail to protect themselves from exposures to toxicants in the workplace or to medications that could damage a developing embryo.

In summary, the timing of implantation varies widely in its relation to the expected period. Many women will test positive a week or more before their period is expected, while a few women will test positive only a week or more afterward. Adolescents and young women are frequent users of test kits¹⁴ but may be especially prone to false-positive test results because they are at

high risk for delayed ovulation.¹⁵ Better information on the limits of early testing can help balance the costs and benefits of early detection against the risks of a false-negative test result.

Author Contributions: Study concept and design: Wilcox.

Acquisition of data: Wilcox, Baird, McChesney, Weinberg.

Analysis and interpretation of data: Wilcox, Baird, Dunson, McChesney, Weinberg.

Drafting of the manuscript: Wilcox.

Critical revision of the manuscript for important intellectual content: Wilcox, Baird, Dunson, McChesney, Weinberg.

Statistical expertise: Dunson.

Administrative, technical, or material support: Wilcox, McChesney.

Study supervision: Wilcox.

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PMA
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Conceptus Essure™ System
Pre-Market Approval Application
(PMA)

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PMA
Conceptus, Inc.

II. Device Samples

In accordance with a request from the FDA, Conceptus, Inc. is providing two samples of the Essure System. These samples are provided with this PMA application.

Exhibit 4 - Rationale for Change in 3-month Post-Procedure Follow-up

(b)(4)



Exhibit 4 - Rationale for Change in 3-month Post-Procedure Follow-up

(b) (4)



Evaluation of Falope Ring Sterilization by Hysterosalpingogram

Christine L. Cook, M.D.

One hundred eight women sterilized by laparoscopically directed application of Falope Rings were evaluated by postoperative hysterosalpingography (HSG). Operations were performed from November 1975 through March 1977 at Louisville General Hospital, Louisville, Kentucky, by residents in obstetrics and gynecology. Local anesthesia was used for 30% of the procedures; general endotracheal anesthesia was used for the remainder. Xylocaine jelly was placed on each ring prior to its application. HSG was done on each woman at least three months following surgery. In three cases extravasation from one tube occurred. None of the women had extravasation from both tubes. One patient with intraabdominal spill had a repeat sterilization by laparoscopic cauterization. The remaining two patients, who have been followed for three years, have not used contraception and have not conceived. The clinical significance of ex-

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LATE TUBAL PATENCY FOLLOWING TUBAL LIGATION*

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Hysterosalpingography (HSG), performed in the first 3 months after tubal ligation, has demonstrated a 1% to 2% incidence of tubal patency when initial operative errors have been excluded. In a group of 54 women, HSG was performed a mean of 4.8 years following sterilization; 9 women (16.7%) demonstrated spillage which was confirmed at laparoscopy in 7 of 8 women operated upon. No cases were due to initial surgical error. Delayed acquisition of tubal patency may explain late failure of tubal ligation, and the abnormal tubal lumen formed may be responsible for the increased percentage of ectopic pregnancies observed among sterilization failures. Ectopic pregnancy must be strongly considered in any failure of tubal ligation. In investigating the proximal tubal segment prior to consideration for tubal reconstruction, the possibility of a pre-existing or an iatrogenically formed fistula must be recalled which may predispose the patient to ectopic pregnancy.
Fertil Steril 35:406, 1981

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*The opinions expressed in this paper are those of the author and do not represent the Bureau of Medicine and Surgery, the Department of the Navy, or the Department of Defense.

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Hysterosalpingographic follow-up of laparoscopic sterilization

HAMID H. SHEIKH, M.D.

Louisville, Kentucky

Two hundred and fifty of 323 laparoscopically sterilized patients had hysterosalpingographic (HSG) follow-up. A Foley catheter was used in hysterosalpingography. Of these patients, 3.6 per cent demonstrated fistula; 1.2 per cent were found to have round ligament burns, and 0.618 per cent became pregnant. Mechanism of fistula formation, prevention, and management is discussed. The incidence of intrauterine pregnancy and ectopic pregnancy after laparoscopic sterilization is discussed, and the literature is reviewed. Based on these data, it is concluded that HSG follow-up is helpful in teaching institutions and where the laparoscopic sterilization is carried out by inexperienced operators. Routine HSG follow-up is not recommended.

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Hysterosalpingographic follow-up of the partial salpingectomy type of sterilization

HAMID H. SHEIKH, M.D.

Louisville, Kentucky

Two hundred and eleven of 743 patients with salpingectomy-type sterilization had hysterosalpingographic (HSG) follow-up. This type of sterilization was performed post partum, electively suprapubic, vaginally (including fimbriectomies), or at the time of cesarean section. A Foley catheter technique was used for hysterosalpingography. Of these, 1.895 per cent had fistula on hysterosalpingography. Mechanism of fistula formations and recanalization is discussed. A modification of the Pomeroy sterilization procedure is described and discussed. (AM. J. OBSTET. GYNECOL. 128: 868, 1977.)

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IV. Professional Training Program

This section provides an outline of the proposed Physician Training Program as well as draft materials intended for use in the Training Program.

A. Physician Training Program Outline

Table 1 below provides an overview of the Physician Training Program, and **Tables 2** through **5** below provide an outline of the components of the Training Program: 1) Physician Training Manual, 2) Physician Training Presentation, 3) Model Training, and 4) Preceptored Cases. A summary of results obtained to date during commercial use with this type of training program outside of the United States are provided in **Exhibit A**. A copy of the draft Training Manual is provided as **Exhibit B**.

(b)(4)



V. Environmental Assessment

Under 21 CFR §25.34(d), Conceptus, Inc. claims a categorical exclusion from the requirement that an environmental impact be performed.

VI. Financial Disclosure and Certification


In accordance with 21 CFR 814.20(b)(12), Conceptus is making financial certification and disclosure statements for its Peri-hysterectomy study, Pre-hysterectomy study, Phase II Trial and Pivotal Trial, in accordance with the provisions of 21 CFR 54. The following physicians served as Investigators for these trials. These study data are being used in support of this marketing application submitted to the Agency by Conceptus Incorporated.

Investigator

(b) (6)



(b)(4), (b)(6)



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Conceptus Incorporated has acted with due diligence to obtain the information required under 21 CFR 54.4. As such, Conceptus hereby discloses the following required financial information.

Employee Information

During the course of the clinical study, none of the Investigators were a full-time or a part-time employee of Conceptus Incorporated.

Compensation Affected by the Outcome of Clinical Studies

(b)(4), (b)(6)




Proprietary Interest in the Tested Product

None of the Investigators, the Investigator's spouses, or their dependent children held or received a proprietary interest in the tested product during the course of the study.

Significant Equity Interest in the Sponsor of Covered Clinical Study

(b)(4), (b)(6)




Significant Payments of Other Sorts

(b)(4), (b)(6)




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(b)(4), (b)(6)



Steps Taken to Minimize the Potential for Bias

(b)(4), (b)(6)



Financial Certification/Disclosure Forms

Financial information relating to Conceptus clinical studies was collected from each Investigator. Included in **Appendix A**, are the following FDA Forms signed by the Vice President of Regulatory Affairs at Conceptus Incorporated.

Form FDA 3454 – Certification: Financial Interests and Arrangements of Clinical Investigators;

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PMA
Conceptus, Inc.

And

Form FDA 3455 – Disclosure: Financial Interests and Arrangements of Clinical Investigators.

A copy of the applicable Conceptus SOP is located in **Attachment B** (SOP-2021/Clinical Study- Investigator Financial Disclosure).

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TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

(b) (6)

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME (b) (6)	TITLE (b) (6)
FIRM/ORGANIZATION Conceptus Incorporated 1021 Howard Avenue San Carlos, CA 94070	
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Please mark the applicable checkbox.

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Please mark the applicable checkbox.

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(b) (6)

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
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The following information concerning (b) (6), who participated as a clinical investigator in the submitted study Phase II and Pivotal trials for *Name of*
Conceptus Incorporated, is submitted in accordance with 21 CFR part
clinical study
54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME (b) (6)	TITLE (b) (6)
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TO: (b) (6)

The following information concerning _____, who participated as a clinical investigator in the submitted study _____ Phase II and Pivotal trials for _____ Conceptus Incorporated _____, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
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- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

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The following information concerning (b) (6), who participated as a clinical investigator in the submitted study Phase II and Pivotal trials for (b) (6), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME (b) (6)	TITLE (b) (6)
FIRM/ORGANIZATION Conceptus Incorporated, 1021 Howard Avenue, San Carlos CA 94070	
SIGNATURE (b) (6)	DATE 4-12-2009

Paperwork Reduction Act Statement

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Rockville, MD 20857

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning (b) (6), who participated as a clinical investigator in the submitted study Pivotal trial for Conceptus Incorporated, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME (b) (6)	TITLE (b) (6)
FIRM/ORGANIZATION Conceptus Incorporated, 1021 Howard Avenue, San Carlos CA 94070	
SIGNATURE (b) (6)	DATE 4-12-2002

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Expiration Date: 3/31/02

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning (b) (6), who participated as a clinical investigator in the submitted study Pivotal trial for Conceptus Name of clinical study Incorporated, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME (b) (6)	TITLE (b) (6)
FIRM/ORGANIZATION Conceptus Incorporated, 1021 Howard Avenue, San Carlos CA 94070	
SIGNATURE (b) (6)	DATE 4-12-2002

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Rockville, MD 20857

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CLINICAL STUDY – INVESTIGATOR FINANCIAL DISCLOSURE

SOP-2021

Revision Level	ECO#	Effective Date	Originators Name	Change Request
A	(b)(4)	2/14/02	(b) (6)	Initial Release

CONTROLLED DOCUMENT

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