P020014 R12 C1

P020014/R12/C1

Conceptus.

June 19, 2006

Colin M. Pollard, Branch Chief, Obstetrics and Gynecology Branch
Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, MD 20850

Re: **Phase II Clinical Study Final Report**
submitted in partial fulfillment of Post Approval Requirement #1
PMA P020014, Conceptus Essure® System for Permanent Birth Control

Dear Mr. Pollard,

Conceptus is pleased to submit this Phase II Clinical Study Final Report in partial fulfillment of the post approval requirement #1 (as listed on the PMA approval letter, dated November 4, 2002). The attached Report includes patient follow-up data to 5 years as well as a summary and conclusion.

The Final Report is comprised of the following Exhibits:

Exhibit 1: Copy of the PMA approval letter, dated November 4, 2002
Exhibit 2: Phase II Clinical Study Final Report
Exhibit 3: Phase II Study Protocol

Please let me know if you have any questions or need additional information. I can be reached by phone at (650) 962-4170, by fax at (650) 691-4729, or by email at esinclair@conceptus.com. Please note the new address and contact information below.

Sincerely,

Edward J. Sinclair
Vice President, Clinical Research, Regulatory Affairs and Quality Assurance
Conceptus, Inc.
331 E. Evelyn Ave.
Mountain View, CA 94041 USA
Direct: (650) 962-4170
Fax: (650) 691-4729

Exhibits: 1-3

FEB 15 2007

Mr. Edward Sinclair
Vice President, Clinical Research, Regulatory Affairs
and Quality Assurance
Conceptus, Inc.
331 E. Evelyn Ave.
MOUNTAIN VIEW CA 94041

Re: P020014/R012
Conceptus Essure® System for Permanent Birth Control
Received: June 20, 2006
Amended: December 4, 2006

Dear Mr. Sinclair:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your FINAL REPORT for your postapproval study for your premarket approval application (PMA) for the Essure® System for Permanent Birth Control. The specific conditions for the postapproval study were described in your approval order dated November 4, 2002, for P020014.

We are pleased to inform you that we now consider these conditions satisfied. You are required to continue to report in accordance with the requirements of 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

1. Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

2. Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

   a. unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

   b. reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

If you have any questions concerning this letter, please contact Ms. Elaine Blyskun at (240) 276-4100.

Sincerely yours,

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

cc: HFZ-402 (PMA Staff)
HFZ- 470 (DRARD)
HFZ-542 (Statistics Staff)
HFZ–541 (Loyo-Berrios)
D.O.

DRAFT:ElaineBlyskun:2.12.2007
FINAL:ElaineBlyskun:lrm:2.12.2007

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
~~2490~~	Blyskun	02.12.07	Z-470	Segroves	2/14			
Z470	Gamble	2-12-07						
Z470	Pollard	2/12/07						

U.S. GPO 1986-169-089

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

FEB 15 2007

Mr. Edward Sinclair
Vice President, Clinical Research, Regulatory Affairs
and Quality Assurance
Conceptus, Inc.
331 E. Evelyn Ave.
MOUNTAIN VIEW CA 94041

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Received: June 20, 2006
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If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

If you have any questions concerning this letter, please contact Ms. Elaine Blyskun at (240) 276-4100.

Sincerely yours,

for Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

EXHIBIT 1

Copy of PMA P020014 Approval Letter
Dated November 4, 2002

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Cindy Domecus
Senior Vice President
Clinical Research and Regulatory Affairs
Conceptus, Inc.
1021 Howard Avenue
San Carlos, California 94070

NOV - 4 2002

Re: P020014
Essure™ System
Filed: April 22, 2002
Amended: May 3, 16, 28, June 7, 13, 24, July 18, 22, August 21, 23,
September 4, 16, 23, 27, 30, and October 16, 18, 21 and 22, 2002.
Procode: 85 HHS

Dear Ms. Domecus:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Essure™ System. This device is indicated for permanent birth control (female sterilization) by bilateral occlusion of the fallopian tubes. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions described below and in the "Conditions of Approval" (enclosed).

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specifies the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the post approval requirements outlined in the enclosure, you have agreed to provide the following data in post approval reports:

1. 5-Year Follow-up under Phase II and Pivotal Trials

In order to gather long-term safety and effectiveness data on the Essure™ System, you are required to follow participants who are not relying on Essure™ for contraception for safety evaluation only, at 2, 3, 4, and 5 years after *implantation*. You are required to follow

participants who are relying on Essure for contraception for both safety and effectiveness at 2, 3, 4, and 5 years after *discontinuation of alternative contraception.* Data collected should include the following:

a. pregnancies and outcomes;

b. adverse events; and,

c. histological explant data following any extirpative surgeries, if available.

Reports must be submitted annually. When a full five-year follow-up report is submitted, FDA will determine if continued follow-up of these study subjects is required. Please be advised that the results from this follow-up must be included in the labeling as these data become available. Potentially, this could mean that annual revisions to the labeling will be necessary. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

2. Post approval study in the U.S. with newly trained physicians.

This study is intended to document the bilateral placement rate for newly trained physicians (800 patients, 40 physicians, first 20 attempts). These data will be used to evaluate the training procedures and to update labeling. Data collected should include the following:

a. rates of successful bilateral placement of the Essure™ System at first attempt; and

b. identification of factors predictive of failure to achieve bilateral placement of the Essure™ System at first attempt.

Expiration dating for this device has been established and approved at nine months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

CDRH does not evaluate information related to contract liability warranties, however you should be aware that any such warranty statements must be truthful, accurate, and not misleading, and must be consistent with applicable Federal and State laws.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at http://www.fda.gov/cdrh/pmapage.html. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an

independent advisory committee, under section 515(g) of the Federal Food, Drug and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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

If you have any questions concerning this approval order, please contact Ms. Lisa Lawrence at (301)594-1180.

Sincerely yours,

Daniel G. Schultz, M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure
Conditions of Approval

Last Modified: 1-31-02

CONDITIONS OF APPROVAL

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e) or (f). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations that require a PMA supplement cannot be briefly summarized; therefore, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report (see below). FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

Alternate submissions permitted under 21 CFR 814.39(f) for manufacturing process changes include the use of a 30-day Notice. The manufacturer may distribute the device 30 days after the date on which the FDA receives the 30-day Notice, unless the FDA notifies the applicant within 30 days from receipt of the notice that the notice is not adequate.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

1. Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

2. Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

   a. unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

   b. reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

1. A mix-up of the device or its labeling with another article.

2. Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and:

   a. has not been addressed by the device's labeling; or

   b. has been addressed by the device's labeling but is occurring with unexpected severity or frequency

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336)and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers International and Consumer Assistance (DSMICA) at 301-443-8818.

EXHIBIT 2

Phase II Clinical Study Final Report

Conceptus®

CLINICAL DATA FINAL REPORT: PHASE II STUDY

Prepared for the annual update to PMA P020014

Data current to January 6, 2006

Table of Contents

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Exhibits

Figures

Tables

(b)(4)

A. Background

This section reports the data obtained from the Phase II study, IDE #G980152. (b)(4) design concepts clinically evaluated during the development of the Essure Micro-insert (see **Device Description, PMA Module I**) were tested in the Phase II study. Specifically, the following design concepts were evaluated: (b)(4) . (b)(4) The IDE for the Phase II study was submitted on June 19, 1998, conditionally approved on July 22, 1998, and fully approved on October 9, 1998. (b)(4) (b)(4) . The IDE supplement for the (b)(4) was submitted on December 17, 1998, conditionally approved on January 19, 1999[1], and fully approved on March 26, 1999. The PMA was approved by FDA on November 4, 2002. Since PMA approval was for the (b)(4) design, this section reports detailed results for the (b)(4) design only. A brief summary of the results for the other designs can be found in **Exhibit A.**

The data in this report are current to January 6, 2006.

B. Study Purpose and Protocol

This was a prospective, multi-center, international study of women seeking permanent contraception. Investigational sites were located in the United States, (b)(4) . All sites conducted the study according to virtually the same protocol as that approved under the IDE (previously submitted in the PMA Amendment dated October 15, 2002, Module 5, Volume 1, Exhibit E), and obtained approval from an Institutional Review Board (IRB) or Ethics Committee (EC) before study commencement. A protocol revision history is provided in **Exhibit B.**

All sites were monitored according to the same standard operating procedures in accordance with the U.S. Good Clinical Practice 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.

(b)(4)

Screening

Women who read and signed the Informed Consent Form were interviewed for demographic and socioeconomic data. (b)(4)

(b)(4)

Placement procedure

(b)(4)

Follow-up procedures

(b)(4)

(b)(4)

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

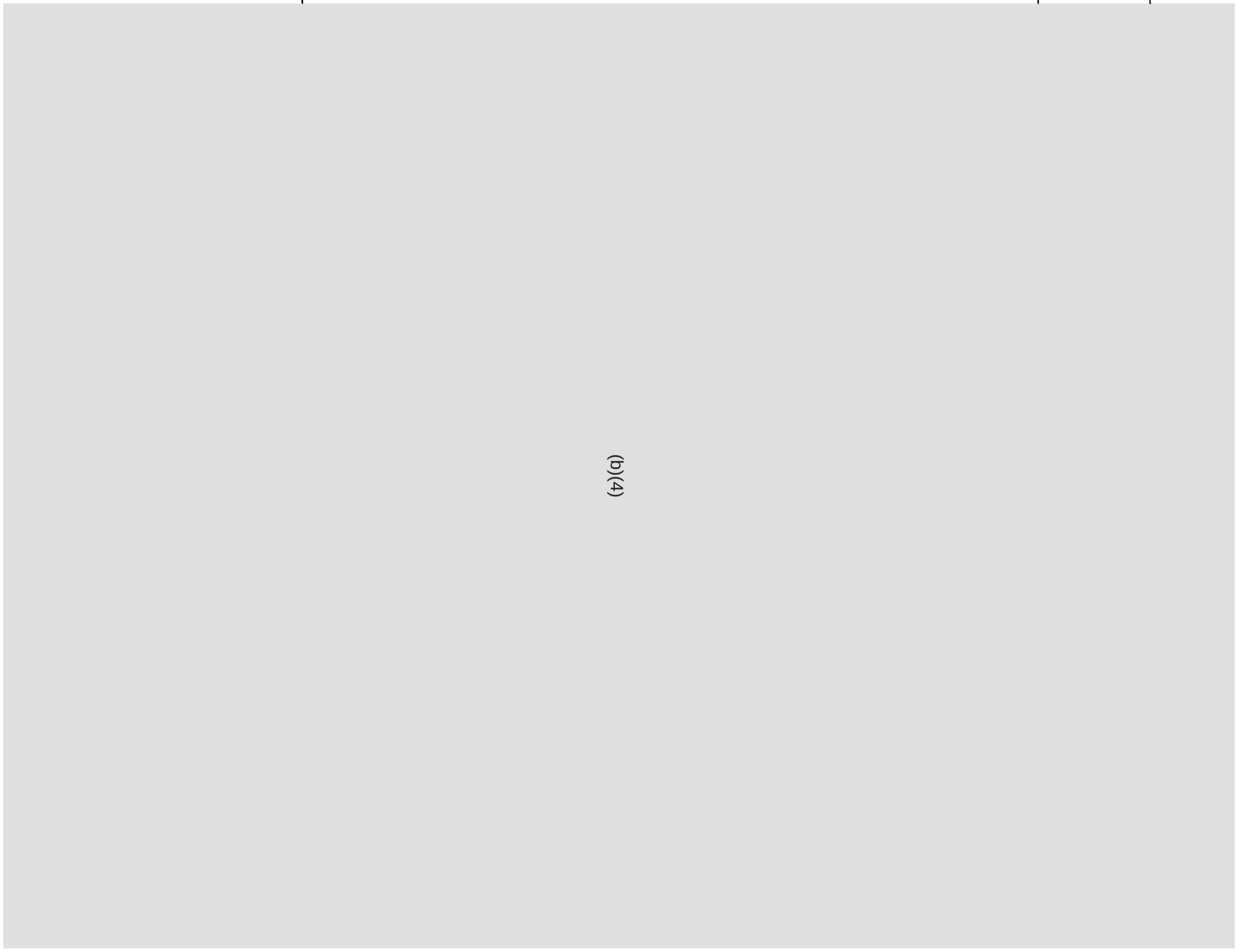
D. Number of Investigators/ Subjects per Investigator

Investigators participating under the IDE were located in the United States.

(b)(4)

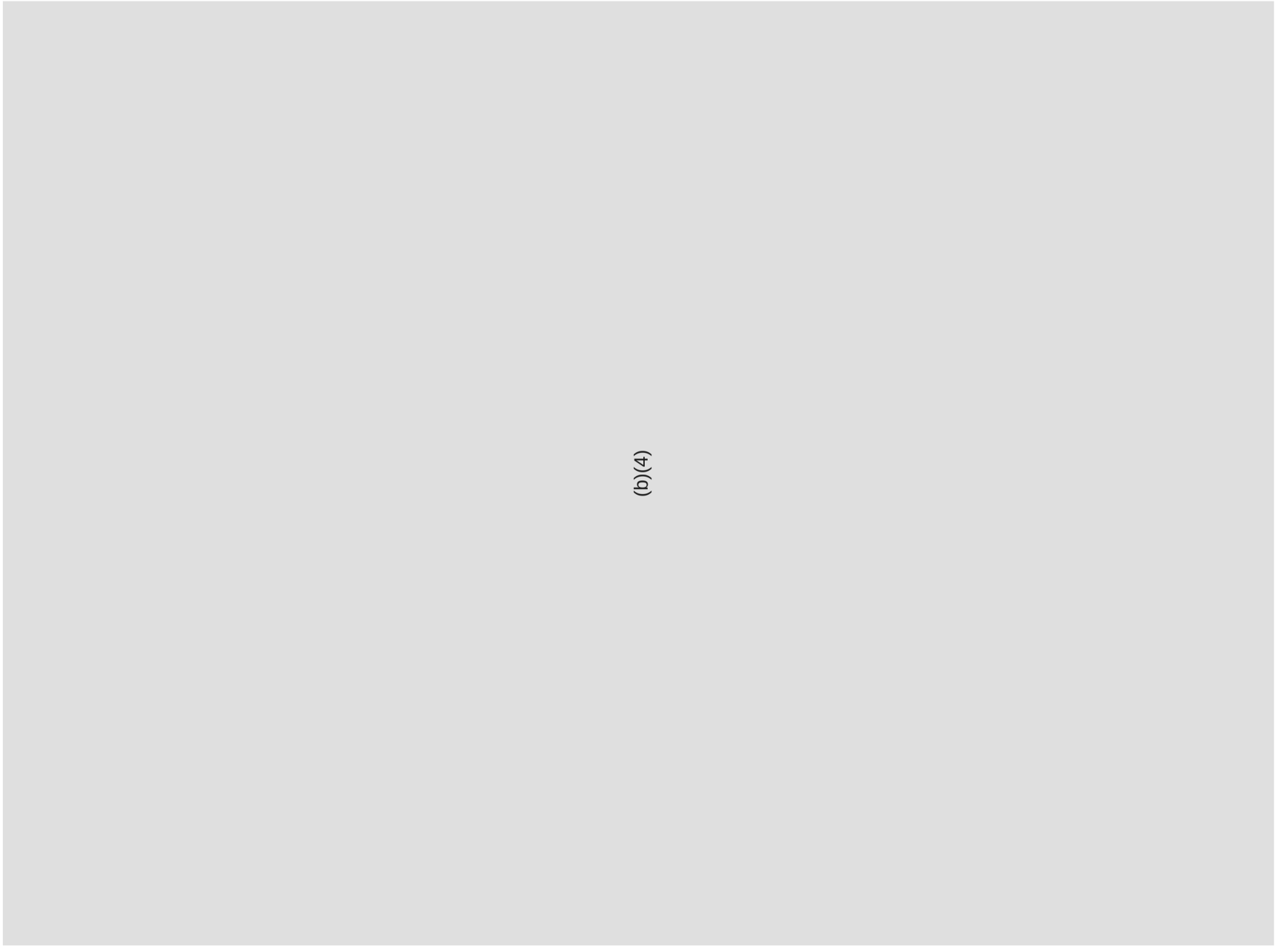
Table II.1: Distribution of Investigators/ Number of Women Undergoing Placement

Investigator	Number of Women
USA	(b)(4)
Other countries	(b)(4)
	(b)(4)
Total	**227**


(b)(4)

F. Patient Tree

Figure II.1. Patient Accountability Tree



G. Study Demographics

The average age of the women undergoing device placement was (b)(4) with a range of (b)(4) **Table II.2** below provides the age distribution. Other demographics are in **Table II.3**.

Table II.2: Age Distribution at time of Essure placement

N=227 mean=(b)(4) (Range= (b)(4)

Age	Number	Percent
(b)(4)		

Table II.3: Demographics

(N=(b)(4)

Demographic	Mean	Median	Std deviation
Height	(b)(4)		
Weight			
Gravidity			
Parity			
Completed high school			

H. Micro-insert Placement Rate

Of the 227[5] women who underwent a procedure, bilateral Micro-insert placement was achieved in 200/227 women (88%). Unilateral placement was achieved in 6/227 (3%). (b)(4) of the women in whom bilateral placement was achieved required 2 visits to achieve bilateral placement. (b)(4) women underwent a second procedure but did not achieve bilateral placement. These data are provided in **Table II.4** below.

(b)(4)

Table II.4: Micro-insert Placement Rates

Placement status	Number	Percent
Women Undergoing Procedure	227	
Micro-insert Placement:		
Bilateral Micro-insert Placement	200	88%
Achieved after 1 procedure		
Achieved after 2 procedures		
Unilateral Micro-insert Placement	6	2%
Bilateral Failure	21	10%

In twenty-seven women bilateral Micro-insert placement was not achieved. Reasons for failure to place Micro-inserts bilaterally are summarized in **Table II.5**.

Table II.5: Reasons for Failure of Bilateral Micro-insert Placement- Includes Reasons for Failure in First and Second Procedures

Reason for placement failure	Number	Percent
(b)(4)		
Total	27	100%

(b)(4)

Procedure Time

The time required for completion of the Micro-insert placement procedure was calculated in the study as time of insertion of the hysteroscope until removal. The average procedure time was (b)(4) minutes for all procedures, and (b)(4) minutes for procedures with bilateral placement.

I. Safety/Comfort of Micro-insert Placement Procedure

Anesthesia

(b)(4)

Table II.6: Predominant Anesthesia Used
(Includes first and second procedures)

Anesthesia	Number	Percent
(b)(4)		
Total	(b)(4)	

(b)(4)

Adverse events

(b)(4) women (<1%) experienced an adverse event on the day of the procedure. (b)(4) women had vaso-vagal responses that were treated with atropine, one (b)(6) resolved immediately and one (b)(6) required observation for several hours prior to discharge. (b)(4) woman (b)(6) complained of severe leg pain during the procedure that was likely due to positioning. The pain was resolved within 2 hours with analgesics and a change in position.

(b)(4) woman (b)(6) complained of severe post-op pain. This may have been related to Micro-insert deployment in the fallopian tube. The pain resolved with analgesics within 8 hours following the procedure.

In (b)(4) women (b)(6), the proximal band of the Micro-insert became detached during Micro-insert placement and was noted on the x-ray to be

(b)(4)

One-week Questionnaire

One week after Micro-insert placement, women were asked to complete a questionnaire, (b)(4) (b)(4) (b)(4) Two weeks post-Micro-insert placement, women were contacted to assess any adverse events and encourage completion of the patient questionnaire. Patient questionnaires from (b)(4) women undergoing Micro-insert placement were received. The remaining (b)(4) did not complete the questionnaire because they were either a bilateral failure (b)(4) or a unilateral failure (b)(4)

Tolerance of Procedure

(b)(4)

(b)(4)

Post-Procedure Pain

Post-procedure pain was reported in (b)(4) The pain was

(b)(4)

Of those experiencing pain, (b)(4) took medication for the pain. Of the

(b)(4)

Women were asked about activities that elicited pain during the one-week post-placement time frame. **Table II.7** summarizes activities that elicited pain one week following the procedure.

Table II.7. Activities that elicited pain one week following the procedure

Pain	Number	Percent
(b)(4)		

Post-Procedure Bleeding

Post-procedure bleeding was reported in (b)(4) respondents. **Table II.8** summarizes the time to resolution of the bleeding. Most of the bleeding was

(b)(4)

Table II.8. Time to resolution of bleeding

Time	Number	Percent
(b)(4)		

(b)(4)

(b)(4)

(b)(4)

"Other" Symptoms

(b)(4)

J. Safety/Comfort of Micro-insert Wearing

Micro-insert Wearing Data

(b)(4)

Table II.10: Follow-up Status as of January 6, 2006

Follow-up visit	Number completing visit to date
(b)(4)	

A woman's tolerance to wearing Essure was ascertained at the (b)(4) (b)(4) -month follow-up, and has been rated as "good" to "excellent" in 99% of women at all visits. These data are presented in **Table II.11** below.

Table II.11: Tolerance to wearing Essure

Follow-up Time Point	Excellent	Very Good	Good	Fair	No response

(b)(4)

(b)(4)

Table II.12: Pain reported at follow-up visits

Follow-up visit	Pelvic pain			Other Pain
	Dysmenorrhea	Dysparcunia	Other Pelvic	
(b)(4)				

Table II.13 summarizes the unscheduled office visits made by women reporting pain.

Table II.13: Pain reported at unscheduled visits

Pt. No.	Date of Visit	Symptoms reported
(b)(4), (b)(6)		

Table II.14 summarizes the unusual bleeding that women reported. In the first 3 months following discontinuation of alternative contraception (6 months post-procedure), women most commonly reported spotting. At subsequent follow-up visits, irregular menses and changes in flow were more common, though all were reported in (b)(4) or less of women.

Table II.14: Unusual bleeding reported at follow-up visits

Follow-up visit	Irregular menses	Spotting	Changes in flow	Other
(b)(4)				

(b)(4)

Table II.15 summarizes the unscheduled office visits made by women reporting unusual bleeding.

Table II.15: Unusual bleeding reported at unscheduled visits

Pt. No.	Date of Visit	Symptoms reported
(b)(4), (b)(6)		

HSG Results

In the 200 women who initially had bilateral placement and in 2 women who initially had unilateral placement, an HSG was performed to assess tubal occlusion at the 3-month follow-up visit. In addition, assessment of satisfactory Micro-insert location was performed using either HSG or an ultrasonogram (USG). (b)(4)

(b)(4)

group). The HSG findings are provided in **Figure II.2 and Table II.16.**

Figure II.2. HSG Findings

(b)(4)

Micro-insert location

Table II.16 contains information about Micro-insert location for women with initial bilateral placement. Of 200 women with initial bilateral placement undergoing HSG evaluation, 6 (3%) had unsatisfactory Micro-insert location: 3 had unsatisfactory Micro-insert location on the left; 2 had unsatisfactory Micro-insert location on the right; and one woman had bilateral unsatisfactory Micro-insert location. Reasons for unsatisfactory Micro-insert placement are summarized in the adverse event section below, **Table II.17**.

Table II.16: HSG Results for Bilateral Placements, N= (b)(4)

Month of evaluation	Number of women undergoing evaluation	Number of women with satisfactory Micro-insert location	Number with bilateral occlusion	Number with satisfactory Micro-insert location and occlusion	Occlusion in women with satisfactory Micro-insert location
(b)(4)					

Occlusion

Occlusion of the fallopian tubes was evaluated by the 3-month HSG in all (b)(4) omen with bilateral placement and is summarized in **Table II.16** above. Of the (b)(4) omen

(b)(4)

Of the nine women with patency of at least one tube at the time of the 3-month post-procedure HSG, one woman had a unilateral patency due to an expelled Micro-insert and one woman had unilateral patency due to an inadvertent Essure Micro-insert placement in the myometrium instead of the fallopian tube. The remaining seven women who had patency or equivocal occlusion with satisfactory Micro-insert position on the 3-month HSG underwent a repeat HSG at 6 months post procedure. Each of these women had bilateral occlusion on the second HSG.

(b)(4)

In summary, of the (b)(4) initial bilateral placements, (b)(4) 97%) had satisfactorily placed Micro-inserts with occlusion and were subsequently able to rely on the Micro-insert. The other 3% had unsatisfactory device location due to expulsion, perforation or an incorrectly positioned Micro-insert. Of the (b)(4) women with satisfactorily located Micro-inserts, 100% had bilateral occlusion.

Retrospective Analysis of IISGs

(b)(4)

(b)(4)

Adverse Events Reported to October 8, 2002

Adverse events that occurred after the day of the procedure have been reported in 21/227 women (9.3%). Of these, 12/227 (5.3%) are related to episodes of period pain, ovulatory pain or changes in menstrual function. **Table II.17** summarizes the other 9 adverse events that impacted patient reliance, and the patient management for each. In addition, one woman underwent hysterectomy for uterine prolapse that was unrelated to the Essure Micro-insert. However, the surgeon cut through the Essure Micro-insert during the hysterectomy and a small fragment remains in the patient's fallopian tube.

Table II.17: Adverse events

Adverse event	Number	Suspected Cause	Patient management
Unsatisfactory Device Location			
Perforation	7 (3.1%)	Preexisting tubal occlusion (2); perforation with use of the Support Catheter (5)	Laparoscopic sterilization (5) with device retrieval in 3; cornual resection and device removal (1); relied on perforated device (1)
Expulsion	1 (<1%)	Due to initial proximal placement of Micro-insert	Second Micro-insert procedure unsuccessful due to stenotic tube, husband had vasectomy
Other Unsatisfactory Device location	1 (<1%)	Due to initial distal placements of both Micro-inserts	Laparoscopic sterilization, bilateral salpingectomy
Other Events			
Retained Micro-insert fragment	1 (<1%)	Excessive force used during removal attempt, resulting in broken distal ball tip	Repeat x-ray 3-months after procedure showed retained fragment, no further follow-up

Each of these is described in more detail below.

Unsatisfactory Device Locations

Unsatisfactory device (Micro-insert) location (UDL) was noted in 9 women. These consisted of seven perforations, one expulsion and one "other" unsatisfactorily located device. Each is detailed further below.

Expulsion

(b)(4)

Perforations

There were 7 women who were diagnosed with a perforation. (b)(4)

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

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

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

Distal Location

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

Broken Micro-insert tip

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

Unrelated Adverse Events Reported to October 8, 2002

Refer to the Adverse Event data table previously submitted in the PMA Amendment dated October 15, 2002, Module 5, Volume 1, Exhibit D.

Summary of Adverse Events Reported to October 8, 2002

Adverse events impacted the ability to rely on the Essure Micro-insert in 8/200 women with bilateral placement (4.0%). Improved physician training on Micro-insert placement,

(b)(4)

reported in the Pivotal trial). The Support Catheter, which was associated with a high number of the perforations experienced in the early Essure clinical trials, was discontinued during the Phase II trial. (b)(4)

(b)(4)

In summary, the overall adverse event rate in the Phase II study reported to October 8, 2002 was low, with less than 1% of women experiencing an adverse event on the day of the procedure, and less than 4% experiencing an adverse event after the day of the procedure that prevented reliance on Essure. Only two women reported persistent

[8] The Support Catheter was initially used to provide more column strength in difficult procedures. However, it was noted to lead to a higher rate of perforations and was discontinued.

symptoms related to an adverse event, and it is not clear if the symptoms were device-related in either case, since one woman did not experience symptoms until 2 years after wearing the Micro-inserts and the other is having "rare twinges" on the side opposite to the side with the unsatisfactorily located Micro-insert. With the exception of these two women, there have not been any long-term sequelae in women wearing the Essure Micro-inserts.

Adverse Events Reported to January 6, 2006

A table (***Table 1***) provided in ***Exhibit D*** lists all adverse events reported since Phase II study initiation through January 6, 2006. Adverse events are grouped according to their relationship to the Essure device: highly probable, probable, possible, or unlikely. The relationship was rated by each investigator and recorded on the adverse event case report form. On the following page, ***Table II.19*** lists the adverse events that began, ended or were ongoing during the period from October 8, 2002 through January 6, 2006 that were rated by Investigators as having a possible, probable or highly probable relation to the Essure device.

During the final reporting period (10/08/02 to 01/06/06) **there were no adverse events rated by the investigators as 'highly probable' or 'probable' in relation to the study device.** During the same reporting period, **only 3 reported adverse events were 'possibly' attributable to the Essure study device**. A total of 55 adverse events were reported by investigators during this same time period as having an 'unlikely' relationship to the Essure device.

During the past year of follow-up, only 2 patients reported adverse events. (b)(6) (b)(6) was diagnosed with hypermenorrhea that the investigator rated as 'possibly' related to the Essure micro-inserts and (b)(6) had removal of vulval warts that were unrelated to the study device. These events are summarized in ***Table II.18*** below.

Table II.18: AE's that began in the last year of patient follow-up

Pt. No.	Adverse Event	Start Date Stop Date	Severity	Relation-ship to Device	Treatment Required	Other Treatment
(b)(6)	Cautery of vulval warts	(b)(4), (b)(6)	Mild	Unlikely	Other	Burnt off by GP
	Hypermenorrhea		Moderate	Possible	Medication	

The following table (***Table II.19***) lists the adverse events that began or ended during the period from October 8, 2002 through January 1, 2006. Adverse events are grouped according to their relationship to the Essure device: highly probable, probable, possible, or unlikely. The relationship was rated by each investigator and recorded on the adverse event case report form.

Table II.19: AE's that began or ended from 10/08/2002 to 01/06/2006 that are at least "Possibly Related" to Essure

This table is sorted by 'Start Date'

Pt. No.	Adverse Event	Start Date / Stop Date	Severity	Treatment Required	Other Treatment/Outcome
Relationship to study Device = HIGHLY PROBABLE					
(b)(6)	Proximal band detached from device	(b)(6)	Mild	None	Pt is continuing in study with no adverse effects as of 3-yr visit. X-rays are OK.
Relationship to study Device = POSSIBLE					
(b)(6)	Possible ovulation pain reported (b)(6)	(b)(6)	Moderate	Medication commenced (b)(6)	Controlled with medication
	Ovarian discomfort with menses		Mild	None	*Completed 5-year study on* (b)(6)
	Periods heavier and closer together		Mild	None	*Completed 5-year study on*
	Pain on R or L side of pelvis during period		Mild	None	
	Cycle varies between 4-8 weeks		Mild	None	No problems with periods at 3-year visit (b)(6)
	Premenstrual spotting		Mild	Observe and follow-up in 6 months	No spotting as of 3-year visit on (b)(6)
	Cycle irregular		Mild	None	*Completed 5-year study on* (b)(6)
	Heavy periods		Moderate	Medication	Resolved with medication as of 4-year visit (b)(6)
	Period irregular and heavy, lower abdominal pain		Moderate	Laparoscopy and D&C (b)(6)	No pain present as of 4- year visit - (b)(6)
	Hysterectomy for heavy periods		Moderate	Hospitalization	Patient had a hysterectomy and was termed from study (b)(6) per protocol.
	Dysmenorrhea secondary to fibroids		Moderate	Medication	
	Hypermenorrhea		Moderate	Medication	

Patients Having a Hysterectomy

As part of the clinical protocol for the Phase II Study, patients who are scheduled for surgical removal of the fallopian tubes are requested to allow Conceptus to receive, process, and histologically evaluate their tubes. As of January 06, 2006, there were five Phase II Study patients that underwent hysterectomy after Essure placement since study initiation as shown in ***Table II.20*** below. Details are described in the following paragraphs.

Table II.20: Patients having a Hysterectomy from March, 2002 to January, 2006

Pt. No.	Device Placement Date	Date of Hyster-ectomy	Reason for Hysterectomy
(b)(6)			Hysterectomy and repair for vaginal prolapse
			Heavy periods and anemia
			Pelvic pain (endometriosis)
			Dysfunctional uterine bleeding
			Uterine prolapse

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

Hysterectomy Patient (b)(6)

(b)(6)

Hysterectomy Patient (b)(6)

(b)(6)

(b)(6)

Hysterectomy Patient (b)(6)

(b)(6)

Hysterectomy Patient (b)(6)

(b)(6)

(b)(6)

Hysterectomy Patient (b)(6)

(b)(6)

Discussion with Dr. (b)(4), (b)(6)

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

K. Effectiveness

As of January 6, 2006 (the date of the final data extract), the194 women with bilateral placement in the Phase II Study who relied on the micro-inserts for contraception contributed (b)(4) woman-months of effectiveness time without pregnancy. Conceptus intends to submit a PMA supplement later in 2006 that will detail the Phase II and Pivotal Trial effectiveness in order to obtain an updated effectiveness rate claim.

Of the 194 patients that began relying on bilateral Essure micro-inserts for contraception in the Phase II study,(b)(4)women have completed the 5-year follow-up; (b)(4) were lost to follow-up; (b)(4)were being followed for safety reasons only,(b)(4)woman having undergone a tubal ligation and(b)(4)having undergone a hysterectomy (such women still have some portion of the Essure micro-insert in vivo); and(b)(4)had been terminated. (b)(4) because of hysterectomy,(b)(4)because of laparotomy and cornual resection and (b)(4) because they chose, at the two-year study visit, not to consent to continue follow-up for the remainder of the five-year follow-up period and a (b)(4) patient withdrew her consent.

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

Relevant data was recorded on standardized case report forms, a sample of which was previously submitted in the PMA Amendment dated October 15, 2002 (Module 5, Volume 1, Exhibit E) and October 17, 2002 (Volume 1 of 1). (b)(4)

(b)(4) 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 C**.

P. Device Accountability

(b)(4)

Q. Conclusions Drawn From the Study

In the Phase II study, bilateral micro-insert placement was achieved in 200 women and unilateral placement in an additional (b)(4) women. Of these (b)(4) subjects, (b)(4) women have completed the five year study (b)(4) have been lost to follow-up, and (b)(4) were terminated.

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. There were no adverse events between October 8, 2002 and January 6, 2006 that were rated by the Investigator as having a high probability of relating to the Essure device. Furthermore, only three adverse events were reported during the same period that were rated as "possibly" related to Essure.

The primary procedure-related adverse event experienced was perforation (b)(4), (b)(4) Of the perforations, 5/7 (71%) 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 reduced to 1.1% (N=5/476).

A woman's tolerance to wearing Essure was ascertained at the (b)(4) (b)(4) month follow-up, and has been rated as "good" to "excellent" in 99% of women at all visits.

Investigators reported any unusual pain noted by study subjects at each of the follow-up visits. Types of pelvic pain reported most commonly included dysmenorrhea, dyspareunia, and other pelvic pain (mostly ovulation pain). Of the women reporting dysmenorrhea in the first 3 months following the procedure, 11/29 (38%) reported pain in the first week following the procedure and 23/29 (79%) reported pain in the first month following the procedure. It should be noted that of the women reporting dyspareunia in the first 3 months, 8/17 (47%) reported it in the first week following the procedure while 13/17 (76%) reported pain within the first month following the procedure. One woman who reported pain sustained a perforation, with the micro-insert placed in the peritoneal cavity. Women also reported symptoms of pain that were not related to the micro-insert.

For instance, some women reported that their change in dysmenorrhea after the first 3 months was likely related to going off oral contraceptives, given their previous experience with discontinuation of oral contraceptives.

Investigators reported any unusual bleeding noted by study subjects at each of the follow-up visits. In the first 3 months following discontinuation of alternative contraception (6 months post-procedure), women most commonly reported spotting. At subsequent follow-up visits, irregular menses and changes in flow were more common, though all were reported in 9% or less of women.

Persistent pain and bleeding were not reported. Recurrent pain and bleeding were rarely reported. (b)(4) women (b)(4) reported recurrent pain (reported on 2 or more visits that may or may not be consecutive) while persistent pain (reported at every visit) was not reported by any woman. (b)(4) reported recurrent menstrual changes, (b)(4) reported recurrent post-coital bleeding and no women reported persistent menstrual changes.

There were (b)(4) hysterectomies reported in Phase II patients between study initation and completion on January 6, 2006. One woman had a hysterectomy and repair for vaginal prolapse, another had hysterectomy and vaginal vault suspension for uterine prolapse, a third woman underwent hysterectomy for menorrhagia and anemia, a fourth for dysfunctional uterine bleeding probably due to Polycystic Ovarian Syndrome, and a fifth woman had hysterectomy for pelvic pain (endometriosis).

As of their last follow-up contact, there are a total of (b)(4) woman-months of wearing by women with at least one micro-insert implanted (n=206, mean=57.1, SD=14.3) in the Phase II study (excluding Beta designs). As of January 6, 2006 regardless of their last follow-up date, there are a total of (b)(4) woman-months of wearing by women with at least one micro-insert implanted (n=206, mean=74.2, SD=4.8) in the Phase II study. Follow-up visit data are available on (b)(6)

(b)(4)

As of January 6, 2006 (the date of the final data extract), 194 women with bilateral placement in the Phase II Study began to rely on the micro-inserts for contraception and contributed (b)(4) **woman-months of effectiveness time without pregnancy.** Conceptus intends to submit a PMA supplement later in 2006 that will detail the Phase II and Pivotal Trial effectiveness in order to obtain an updated effectiveness rate claim.

Of the 194 patients that began relying on bilateral Essure micro-inserts for contraception in the Phase II study, (b)(4) women have completed the 5-year follow-up; (b)(4) were lost to follow-up; (b)(4) were being followed for safety reasons only, (b)(4) woman having undergone a tubal ligation and (b)(4) having undergone a hysterectomy (such women still have some portion of the Essure micro-insert in vivo); and (b)(4) had been terminated. (b)(4)

because of hysterectomy (b)(4) because of laparotomy and cornual resection and (b)(4) because they chose, at the two-year study visit, not to consent to continue follow-up for the remainder of the five-year follow-up period and a (b)(4) patient withdrew her consent.

In conclusion, the data from this study (in conjunction with the Pivotal Trial data) support the safety, effectiveness, and patient satisfaction with the Essure placement procedure and the implanted micro-insert. Five-year follow-up of patients in this study is complete.

Beta Patients

(b)(4)

EXHIBIT A: SUMMARY OF RESULTS WITH BETA DESIGNS OF THE STOP DEVICE

Summary of results with Beta designs of the STOP device

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

Device Placement and Retention

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

Table 1: Device Placement Rates

Placement status	(b)(4)
Patients attempted	
Device Placement by Patient	
---Bilateral Device Placement	
---Unilateral Device Placement	
---Not successful	

(b)(4)

Device Wearing

Patients returned for visits at (b)(4) months as shown below in **Tables 1 and 2.**

Table 1. Status of Beta patients followed

Patient ID	Placement Status	Follow-up Status
(b)(6)	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Unilateral device with contralateral PTO, chose to rely for contraception	Completed 5 year follow-up
	Became pregnant after 2 years of relying	Voluntary termination prior to 3 year visit
	Unilateral device with contralateral PTO, chose to rely	Voluntary termination just before her 5-year visit (without visit) but was not pregnant on (b)(6)
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Bilateral devices, relied for contraception	Completed 5 year follow-up
	Unilateral device and contralateral patent tube. Followed for safety	Completed 5 year follow-up

Table 2. Beta patients completing follow-up visits

Patient ID	(b)(4)					
	month	**month**	**month**	**month**	**month**	**month**
(b)(6)	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	No	No	No
	Yes	Yes	Yes	Yes	Yes	No
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	Yes	Yes	Yes	Yes	Yes
	Yes	No	Yes	Yes	Yes	Yes
Total no. completing visit	(b)(4)					

(b)(4)

Adverse Events

Device related (or possibly related) adverse events for the 18 women are summarized in **Table 3** below. The last adverse event reported for any Beta patient occurred on January 10, 2004 as listed in **Table 4**.

The same woman (b)(6) who experienced a pregnancy subsequently developed groin pain in October 2001. The devices were removed via laparotomy after four years of implantation, however, according to the operating gynecologist he found it "...difficult to explain how she has left sided and hip pain". (The operating physician's letter regarding the explantation was included in a PMA amendment dated July 17, 2002.) Nevertheless, the patient reported the pain resolved subsequent to device removal.

On gross exam, there was no evidence of granuloma formation or any deformity of the fallopian tube. On histologic examination there was no acute inflammatory infiltrate in the region of the PET fibers, but there was chronic inflammation and dense fibrosis with 100% occlusion of the tubal lumen. There was no evidence of epithelium or lamina propria in the region of the PET fibers, and no evidence of recanalization in this region.

Table 3. Device-related Adverse Events as of January 06, 2006
Beta 1, 2 and 3 combined

Adverse Event Type	Number (Percent)
Pregnancy	1 (5.6%)
Device Expulsion	4 (22.2%)
Unilateral	1 (5.6%)
Bilateral	3 (16.7%)
Device movement	1 (5.6%)
Episode of mild pelvic pain	2 (11.1%)
Mild uterine bleeding / spotting	2 (11.1%)
Severe pelvic/groin pain	1 (5.6%)

Table 4. Adverse events reported to January 06, 2006

Patient ID	Adverse Event	Start Date Stop Date	Severity	Relation-ship to Study Device	Treatment Required	Other Treatment
(b)(6)	Cold/flu	(b)(6)	Mild	None	None	
	Bilateral device expulsion		Severe	Highly probable	Other	Patient informed of laparoscopic clip sterilization.
	Head cold		Mild	None	None	
	Expulsion of STOP device		Severe	Highly probable	Other	Laparoscopic clip sterilization
	Expulsion		Severe	Highly probable	Other	Reinsertion of new STOP devices.
	Sharp pains		Mild	Highly probable	None	
	Uterine bleeding		Mild	Highly probable	None	
	Occasional late periods		Mild	Possible	None	
	Groin pain		Mild	Possible	None	Left device removed on (b)(6)
	Expulsion		Severe	Highly probable	Other	Reinsertion of STOP device
	Upper respiratory infection (URI)		Moderate	Unlikely	Medication	

Table 4 is continued on the next page

Table 4. Adverse events reported to December 15, 2004 (Cont'd)

Patient ID	Adverse Event	Start Date Stop Date	Severity	Relation-ship to Study Device	Treatment Required	Other Treatment
	Movement of one STOP device		Moderate	Highly probable	Other	Laparoscopic bilateral salpingectomy.
	Lower abdominal pain		Mild	Unlikely	None	
	Bleeding/spotting after intercourse		Mild	Possible	None	
	Pregnancy		Severe	Highly probable	Other	Patient planned to continue with pregnancy and successfully delivered
	Right undesirable device location		Moderate	Highly probable	Other	Device removed during hysteroscopy
(b)(6)	Upper respiratory infection	(b)(6)	Mild	Unlikely	Medication	
	Urinary frequency		Moderate	Unlikely	Medication	
	Colposcopy		Mild	Possible	Hospital-ization	
	Dermatitis on forehead		Mild	Unlikely	Medication	*Pt completed 5-year study and was terminated*
	Nonspecific lower abdominal pain		Mild	Unlikely	None	
	Left leg and groin pain		Severe	Probable	Other	Additional tests required to identify device movement - eventually had devices removed on (b)(6)
	Fluid in lungs		Moderate	Unlikely	Medication	

(b)(6) is the previously reported Beta pregnancy patient. She is now terminated from the study.

EXHIBIT B: PHASE II PROTOCOL REVISION HISTORY

PHASE II PROTOCOL REVISION HISTORY[9]

(b)(4)

(b)(4)

Table 1: Group A (b)(6)

(b)(4)

Table 2: Group B – (b)(6)

(b)(4)

Post Placement

(b)(4)

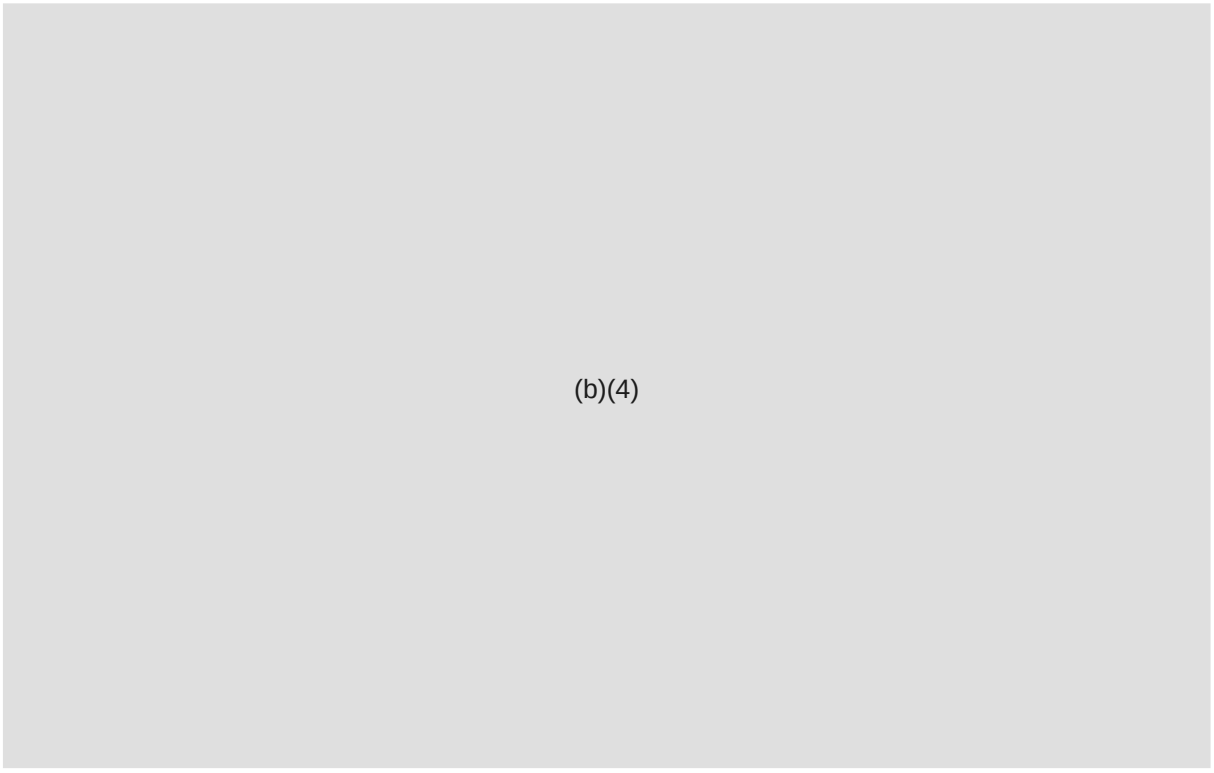

(b)(4)

EXHIBIT C: STUDY DEVIATIONS

EXHIBIT C. STUDY DEVIATIONS

1. Phase II Protocol Deviation Report
Study Initiation to October 8, 2002

Deviations that occurred from the time period of patient screening through the 24-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. The 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 Summary

Type of Deviation	Participants Affected	Percent
Follow-up Schedule Deviations	(b)(4)	
Protocol Deviations		
Informed Consent Deviations		
Inclusion/Exclusion Deviations		
Birth Control Deviations		
Pre-Procedure Testing		
TOTAL		

Follow-up Schedule Deviations

(b)(4)

(b)(4)

(b)(4)

Protocol Deviations

(b)(4)

(b)(4)

Informed Consent Deviations

(b)(4)

Inclusion/Exclusion Deviations

(b)(4)

(b)(4)

Birth Control Deviations

(b)(4)

(b)(4)

(b)(4)

2. Phase II Protocol Deviation Report
October 8, 2002 to November 3, 2003

Deviations that occurred from the time period of the 2-year PAC visit through the 4-year PAC visit are divided into five categories. A summary of the deviation categories is provided below in **Table 2.**

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 (see **Table 3**). The 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 2. Deviation Report Summary (10/08/02 - 11/03/03)

Type of Deviation	Participants Affected	Percent
Follow-up Schedule Deviations*	(b)(4)	
Missed phone contact		
Missed visit and protocol tests		
Lack of notification for hysterectomy		
Had visit or contact, but missed one or more protocol test		
TOTAL	(b)(4)	

Follow-up Schedule Deviations

(b)(4)

(b)(4)

Missed Visit Deviations

(b)(4)

Lack of Notification for Hysterectomy Deviation

(b)(4)

Missed Protocol Test Deviation

(b)(4)

Table 3. Deviation Report Detail (10/08/02 - 11/03/03)

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

3. Phase II Protocol Deviation Report
November 3, 2003 to December 15, 2004

Deviations that occurred from the time period of the 4-year and 5-year PAC visits are divided into five categories. A summary of the deviation categories is provided below in **Table 4.**

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 (see **Table 5**). The 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 4. Deviation Report Summary (11/03/03 - 12/15/04)

Type of Deviation	Participants Affected	Percent
Follow-up Schedule Deviations	(b)(4)	
Missed phone contact		
Missed visit and protocol tests		
Lack of notification for hysterectomy		
Had visit or contact, but missed one or more protocol test		
TOTAL		

Follow-up Schedule Deviations

(b)(4)

Missed Visit Deviations

(b)(4)

Lack of Notification for Hysterectomy Deviation

(b)(4)

Missed Protocol Test Deviation

Twenty-one patients missed one or more protocol tests. These occurred at one clinical site

(b)(4)

Table 5. Deviation Report Detail (11/03/03 - 12/15/04)

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

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

4. Phase II Protocol Deviation Report
December 15, 2004 to January 6, 2006

Deviations that occurred from the time period of the 4-year and 5-year PAC visits are divided into categories. A summary of the deviation categories is provided below in **Table 6.**

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 (see **Table 7**). The 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 6. Deviation Report Summary (12/15/04 - 01/06/06)

Type of Deviation	Participants Affected	Percent
Follow-up Schedule Deviations	(b)(4)	
Had visit or contact, but missed one or more protocol test		
TOTAL		

Follow-up Schedule Deviations

(b)(4)

Missed Protocol Test Deviation

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

Table 7. Deviation Report Detail (12/15/04 - 01/06/06)

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

Table 7. CONT'D

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

5. Phase II Protocol Deviation Report - *October 8, 2002 to January 06, 2006*

(b)(4)

Deviations that occurred from the time period of the 3-year PAC through 5-year PAC visits are listed below in **Table 8.**

Monitoring of the study was detailed and thorough, and included write-ups of any deviation noted, even if minor in nature. The 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 8. Deviation Report Detail (10/08/02 - 01/06/06)

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

EXHIBIT D: ADVERSE EVENTS

EXHIBIT D: ADVERSE EVENTS

Table 1. All reported Adverse Events from Phase II study initiation through 01/06/2006

Pt. No.	Adverse Event	Start Date Stop Date	Severity	Relation-ship to Device	Treatment Required	Other Treatment
(b)(6)	Lower abdominal pain	(b)(6)	Moderate	Highly probable	Other	Devices removed surgically by (b)(6) (b)(6) Pain with periods diminished. Patient is happy with outcome. She was termed with no devices in situ (b)(6) per protocol.
	Rt device placed intra-myometrial		Mild	Highly probable	None	
	Retention of small fragments of STOP device at placement.		Mild	Highly probable	None	Bilateral lap steri was done after failed placement. No second attempt at placement was done. Pt was termed from study on (b)(6)
	Migration of left and right STOP devices		Moderate	Highly probable	Other	Day surgery and laparoscopic bilateral salpingectomy and retrieval of left STOP from peritoneal cavity. Termed from study on (b)(6) per protocol as there were no devices left in situ.
	Uterine perforation		Moderate	Highly probable	Other	Laparoscopy, removal of STOP device from peritoneal cavity. Placed Filshie clip accross L tube.
	L device in peritoneal cavity		Moderate	Highly probable	Other	Laparoscopy and retrieval of L STOP from peritoneal cavity. Bilateral Filshie clips applied.
	L sided device perforated tube device in peritoneal cavity		Moderate	Highly probable	Other	Laparoscopy to retrieve device on (b)(6) -device could not be found. Patient to remain on study to monitor safety of device wearing.
	Proximal band detach from device-visible in uterus via xray		Mild	Highly probable	None	Pt is continuing in study with no adverse effects as of 3-yr visit. X-rays are OK.
	Proximal band detach from device-visible in uterus via xray		Mild	Highly probable	None	Pt is continuing in study with no adverse effects as of 3-yr visit. X-rays are OK.
	Expulsion stop device L tube		Severe	Highly probable	Other	2nd device placement attempt
	Proximal band detached from device		Mild	Highly probable	None	Pt is continuing in study with no adverse effects as of 3-yr visit. X-rays are OK.
	Leg pain		Mild	Highly probable	None	
	Vasovagal reaction		Moderate	Highly probable	Medication	

(b)(6)	Vasovagal reaction	(b)(6)	Moderate	Highly probable	Medication	
	Post op severe pain		Severe	Highly probable	Medication	
	UDI (T tube)		Moderate	Highly probable	Other	Bilateral clip sterlisation (b)(6) (b)(6) Pt is being followed for safety after bilateral clip sterilization.
	R device removed part L devic removed		Mild	Highly probable	Other	Removal of devices during a vaginal hysterectomy and repair. R STOP device and portion of L STOP device removed. Pt to be followed for safety.
	Vaginal discharge		Mild	Possible	None	
	Post-coital bleeding (continuing from previous visit)		Mild	Possible	None	Patient termed after her 2 year visit on (b)(6) because she did not consent > 2 years. She proceeded to tubal ligation at device placement 2 and was followed for Safety.
	Heavy menstrual bleeding		Mild	Possible	None	At her 18 month visit on (b)(6) she reported no unusual bleeding and subsequently LTF
	Ovulatory pain		Mild	Possible	Medication	
	Premenstrual pelvic pain		Mild	Possible	Medication	
	Ovarian discomfort with menses		Mild	Possible	None	Completed 5-year study on (b)(6)
	Heavy periods		Moderate	Possible	Medication	
	Periods heavier and closer together		Mild	Possible	None	
	Pain on R and L side of pelvis during period		Mild	Possible	None	
	Cycle varies between 4-8 weeks		Mild	Possible	None	
	Irregular intermenstrual bleeding		Mild	Possible	Other	Complete diaries for 3 months. Resolved.
	Intermittent bleeding		Moderate	Possible	Medication	Labs drawn Doxycyclene 100 mg tab BID X 7 days return visit
	Premenstrual spotting		Mild	Possible	Other	Observe and follow-up in 6 months. No spotting as of 3-year visit on (b)(6)
	Heavy periods and intramenstrual bleeding		Moderate	Possible	Medication	
	Cycle irregular		Mild	Possible	None	Completed 5-year study on (b)(6)
	Dysmenorrhea		Moderate	Possible	None	Patient did not consent to continue study > 2 years and termed on (b)(6)
	Increase in menstrual flow		Moderate	Possible	None	Patient did not consent to continue study > 2 years and termed on (b)(6)

	Post coital bleeding		Mild	Possible	Other	Complete diaries for 3 months. Resolved.
	Long heavy period		Mild	Possible	None	
	Heavy periods		Moderate	Possible	Medication	
	Dysmenorrhea secondary to fibroids		Moderate	Possible	Medication	No other treatment. Total hysterectomy on (b)(6)
	Period irregular and heavy, lower abdominal pain		Moderate	Possible	Other	Laparoscopy and D and C (b)(6) No pain present as of 4-year visit- (b)(6) (b)(6)
	Pain, heavy bleeding		Moderate	Possible	Medication	
	Hysterectomy for heavy period		Moderate	Possible	Hospitalization	Patient had a hysterectomy and was termed from study (b)(6) per protocol.
	Possible ovulation pain reported 5.31.02		Moderate	Possible	None	Controlled with medication.
	Hypermenorrhea		Moderate	Possible	Medication	
	Ovulation discomfort		Mild	Probable	None	
	Vaginal prolapse		Moderate	Unlikely	Hospitalization	Vaginal hysterectomy and repair.
(b)(6)	Pelvic pain	(b)(6)	Severe	Unlikely	Other	Surgery, pelvic exam (b)(6) revealed probable endometriosis
	Anxiety		Moderate	Unlikely	Medication	(Buspar)
	Paresthesias of R lower leg		Mild	Unlikely	Medication	Ibuprofen
	Sinus infection		Moderate	Unlikely	Medication	(Emycin) pt reported no AE's at 4 mon visit on (b)(6) Therefore, this is the end date of the AE.
	Rt adnexal cystic mass		Severe	Unlikely	Medication	
	Trichomonas		Mild	Unlikely	Medication	Flagyl 500 mg 1 BID for 7 days recovered with tx.
	Ovarian cystectomy		Moderate	Unlikely	Hospitalization	Laparoscopy
	Hot flashes		Mild	Unlikely	Medication	
	Peripheral neuropathy hands and feet		Mild	Unlikely	None	
	U.T.I.		Mild	Unlikely	Medication	
	Abnormal uterine bleeding		Mild	Unlikely	None	NA
	Vaginal infection		Mild	Unlikely	Medication	

	AV nodal Wenckebach		Moderate	Unlikely	Other	Investigation by cardiologist. Patient was fitted with a pacemaker on (b)(6) and is doing fine.
	Infected toe		Mild	Unlikely	Medication	Antibiotics-flucloxocillin 500 mg QID
	Weight gain 25 kgs		Severe	Unlikely	None	
	HTN		Mild	Unlikely	Medication	
	Infection in suture line from previous breast surgery		Mild	Unlikely	Medication	Keflex 500 mg 1 Bd. (b)(6) (b)(6)
	Post coital bleeding		Mild	Unlikely	None	
	Diarrhea		Mild	Unlikely	None	
	Breast tenderness during menstruation		Mild	Unlikely	None	
	Right sided paresthesias		Mild	Unlikely	Other	Referred to psychiatrist and neurologist
	Panic attack		Moderate	Unlikely	Other	Referred to psychiatrist and neurologist
	Cyst on R ovary		Mild	Unlikely	Medication	Panadol 4 hourly and rest. Resolved per ultrasound (b)(6)
(b)(6)	Surgical removal of L wrist lipoma	(b)(6)	Mild	Unlikely	Other	Pt had removal of lipoma's on L wrist as outpatient surgery.
	Bladder infection		Mild	Unlikely	Medication	
	Bronchitis		Mild	Unlikely	Medication	
	Infected ear		Mild	Unlikely	Medication	
	Bronchitis		Mild	Unlikely	Medication	
	Vaginal discharge		Mild	Unlikely	Medication	
	Kidney stone		Moderate	Unlikely	Medication	
	Back pain surgery		Severe	Unlikely	Hospitalization	
	Muscle spasms		Severe	Unlikely	Medication	
	Sinus infection		Moderate	Unlikely	Medication	
	Tonsillitis		Moderate	Unlikely	Medication	Antibiotics
	Contact with HIV blood		Severe	Unlikely	Medication	

	Uterine polyp		Mild	Unlikely	None	
	Urinary tract infection		Moderate	Unlikely	Medication	
	Broken arm		Moderate	Unlikely	Other	Medication for pain and plaster required for broken arm.
	Throat-sinus infection		Moderate	Unlikely	Medication	
	Buccheal abscess		Moderate	Unlikely	Medication	
	Lower abdominal tenderness		Mild	Unlikely	Medication	Participant given prescription for antibioties but did not take them also did not have patholgy tests performed. Feeling a bit better by mid (b)(6)
	Left-ovarian cyst		Mild	Unlikely	Medication	Medication for one month and surgery is now scheduled L oophorectomy.
	Hemorrhagic cystitis		Moderate	Unlikely	Medication	
	U.T.I.		Mild	Unlikely	Medication	
	Hot flushes, mood swings, headachy before periods		Moderate	Unlikely	None	
(b)(6)	Pharyngitis	(b)(6)	Moderate	Unlikely	Medication	
	Headache with menses		Moderate	Unlikely	Medication	
	Frozen shoulder		Severe	Unlikely	Medication	
	Supra pubic pain mideycle ovulation		Moderate	Unlikely	Medication	Observe and review. No pain present as of 3 year visit (b)(6)
	Urinary tract infection		Mild	Unlikely	Medication	
	L calf phlebitis		Moderate	Unlikely	Medication	
	U.T.I.		Mild	Unlikely	Medication	
	Slightly offensive vaginal discharge		Mild	Unlikely	Other	Swabs taken. No discharge at 18 month visit (b)(6)
	Headache		Severe	Unlikely	Medication	
	Vaginitis candidas		Moderate	Unlikely	Medication	
	Migraine		Moderate	Unlikely	Medication	(Advil Migraine) pt began exercising and has not had migraine since
	Skin allergy		Moderate	Unlikely	Medication	

Headache		Mild	Unlikely	Medication	
Headache		Mild	Unlikely	Medication	
L ovarian cyst		Moderate	Unlikely	Medication	
Headache		Moderate	Unlikely	Medication	
Work injury back pain		Moderate	Unlikely	Medication	
Bleeding between periods		Mild	Unlikely	None	
Faringitis		Moderate	Unlikely	Medication	
Rectal fistula		Severe	Unlikely	Hospitalization	Fistula was surgically repaired.
Muscular contracture		Moderate	Unlikely	Other	Physiotherapy, medication
Headache		Moderate	Unlikely	Medication	
L oophorectomy		Moderate	Unlikely	Hospitalization	
Candidiasis		Moderate	Unlikely	Medication	
Anxiety	(b)(6)	Mild	Unlikely	Medication	
Tooth pain		Moderate	Unlikely	Medication	
Hot flushes or irregular cycles		Severe	Unlikely	None	
Tonsillitis		Moderate	Unlikely	Medication	Antibiotics
Occasional spotting for 1 day 2 months ago		Mild	Unlikely	None	
Depression		Moderate	Unlikely	Medication	Recovery, med. were d cd (b)(6)
Eye infection		Mild	Unlikely	Medication	
Breast reduction		Mild	Unlikely	Hospitalization	
RIF pain for 3 months		Mild	Unlikely	None	Period pain-not concerned.
Non malignant tumour on adrenal gland		Moderate	Unlikely	Other	Medication for hypertension. Ultimately lead to hospitalization for removal of tumour. See R adrenalectomy AE.
Kidney infection		Moderate	Unlikely	Medication	
Pelvic pain		Moderate	Unlikely	Medication	

	Muscular pain		Mild	Unlikely	Medication	
	Cold		Mild	Unlikely	Medication	
	Uterine prolapse		Mild	Unlikely	Other	Physiotherapy
	Uterine prolapse		Moderate	Unlikely	Hospitalization	Hysterectomy
	Not sexually active		Mild	Unlikely	None	Hysterectomy and Termination on (b)(6)
	Depression		Mild	Unlikely	Medication	
	Depression		Moderate	Unlikely	Medication	
	Gastric ulcer		Moderate	Unlikely	Medication	
	Bronchitis		Mild	Unlikely	Medication	
	Spastic colon		Moderate	Unlikely	None	
	T.M.J.		Moderate	Unlikely	Medication	
	Intermenstrual bleeding		Mild	Unlikely	Other	Examine and observe. Resolved without treatment.
(b)(6)	Ear infection	(b)(6)	Mild	Unlikely	Medication	
	Vaginal yeast infection		Mild	Unlikely	Medication	
	Bronchitis		Moderate	Unlikely	Medication	
	Spotting after intercourse		Mild	Unlikely	Other	Visit to GP for assessment and Pap smear. No partner since (b)(6) (b)(6)
	Lower abdominal pain possibly bowels.		Moderate	Unlikely	Medication	
	Abdominoplasty		Mild	Unlikely	Hospitalization	
	Frequent heavier periods		Mild	Unlikely	Medication	Resolved with comencement of vitamin B.
	Cycle now varies from 28-35 days		Mild	Unlikely	None	
	Hemorrhoidectomy		Moderate	Unlikely	Other	Outpatient surgery
	Bronchitis		Mild	Unlikely	Medication	
	Polymenorrhea		Mild	Unlikely	None	
	Sinus infection		Mild	Unlikely	Medication	

	Decreased libido since placement	Mild	Unlikely	None	
	Vaginal yeast infection	Mild	Unlikely	Medication	
	Irregular periods	Mild	Unlikely	None	
	Back strain	Mild	Unlikely	Medication	
	Tonsillitis	Mild	Unlikely	Medication	
	Cervicalgia	Mild	Unlikely	Medication	
	Adrenal vein sampling	Mild	Unlikely	Hospitalization	See R adrenalectomy AE.
	Cough sinus infection	Mild	Unlikely	Medication	
	Torn achilles tendon	Moderate	Unlikely	Hospitalization	Plaster
	Varicose veins	Mild	Unlikely	Hospitalization	Varicose veins removed.
(b)(6)	10 teeth removed	Moderate	Unlikely	Other	Hospitalization for removal of teeth. Teeth in poor health due to childhood illness so had them removed. Now taking fungus lozenges.
	Faringitis	Moderate	Unlikely	Medication	
	Dysfunctional uterine bleeding	Moderate	Unlikely	None	
	Depression	Moderate	Unlikely	Medication	
	Bronchitis	Moderate	Unlikely	Medication	
	Vaginal pruritus	Mild	Unlikely	Medication	
	30 min, intermit R side ovarian pain-similar to period pain	Mild	Unlikely	Other	Went to GP-had ultrasound nil found. Pain now gone.
	Phlebitis calf	Mild	Unlikely	Medication	
	Bronchitis	Moderate	Unlikely	Medication	
	Abdominal swelling, especially noticeable during intercourse	Mild	Unlikely	None	
	Polycystic ovarian syndrome (PCOS)	Moderate	Unlikely	Medication	Controlled with medication and naturopathy.
	Hip replacement	Moderate	Unlikely	Hospitalization	Hip was successfully replaced.

(b)(6)	Rhinoplasty and liposuction	(b)(6)	Moderate	Unlikely	Hospitalization	
	Hypothyroid		Mild	Unlikely	Medication	No other treatment recommended
	Fell down steps		Moderate	Unlikely	Medication	
	Sinus infection		Moderate	Unlikely	Medication	
	Cut thumb		Moderate	Unlikely	Other	4 stitches with local doctor
	Flu symptoms		Mild	Unlikely	Medication	
	Bulky uterus		Mild	Unlikely	Other	CT scan, ultrasound scan, visit to Prof Kerin follow-up in 3 months. Uterus normal in size on ultrasound.
	Headaches		Mild	Unlikely	Medication	
	Chicken pox		Moderate	Unlikely	None	
	Cold		Mild	Unlikely	Medication	
	R filshie clip now on L side of pelvis		Mild	Unlikely	None	
	Moodiness		Moderate	Unlikely	None	
	Back injury from fall		Moderate	Unlikely	Medication	#3 physical therapy for one month.
	Post coital bleeding		Moderate	Unlikely	Hospitalization	
	Abscess in tooth		Moderate	Unlikely	Medication	
	Cold		Mild	Unlikely	Medication	
	R adrenalectomy		Severe	Unlikely	Hospitalization	Recovered with treatment-stopped medication on (b)(6)
	Disuria		Mild	Unlikely	Medication	
	Otitis		Moderate	Unlikely	Medication	
	Irregular cycle		Mild	Unlikely	Other	Insertion of Mirena IUCD and D and C
	Anxiety		Moderate	Unlikely	Medication	
	Uterine fibroid		Moderate	Unlikely	Medication	
	Ameloidkesis		Severe	Unlikely	Other	Tumour removed from eye
	2 episodes of midcycle spotting		Mild	Unlikely	Other	Suggest she have pap smear. No further episodes as of (b)(6) (b)(6)

	Pelvic pain (possible adenomyosis)		Moderate	Unlikely	None	
	Shoulder manipulation for frozen shoulder		Moderate	Unlikely	Hospitalization	Hospitalization for shoulder manipulation. Shoulder was unfrozen with manipulation.
	Bursitis R sholder		Severe	Unlikely	Medication	
	Urinary tract infection with every period		Moderate	Unlikely	Medication	UTI's resolved with cystoscopy on (b)(6)
	Sebacous cyst removed		Moderate	Unlikely	Other	Removed in doctors surgery-sutures
	Fibromialgia		Moderate	Unlikely	Medication	
	Pneumonia		Moderate	Unlikely	Medication	
	Back pain		Mild	Unlikely	Medication	
	Cartilage removal knee surgery		Moderate	Unlikely	Other	Surgery
	Right filshie clip now on L. side of pelvis		Mild	Unlikely	None	Pt is being followed for safety only.
	Pulled muscle in abdomen		Moderate	Unlikely	Other	Abdominal ultrasound, ba enema
(b)(6)	Depression	(b)(6)	Moderate	Unlikely	Medication	Medication is Zoloft.
	L. pelvic pain which is intermittent		Mild	Unlikely	None	
	Irregular periods		Moderate	Unlikely	Medication	
	Pneumonia		Moderate	Unlikely	Hospitalization	Resolved with medication.
	R sided pain for six months		Mild	Unlikely	None	
	Stress		Mild	Unlikely	Medication	
	Headaches		Moderate	Unlikely	Other	Changed antidepressants
	2nd hip replacement		Severe	Unlikely	Hospitalization	Second hip was successfully replaced.
	Nausea and vomiting with period		Severe	Unlikely	Hospitalization	
	Endometrial polyp		Moderate	Unlikely	Hospitalization	Polyp removed.
	Bipolar episode		Moderate	Unlikely	Medication	
	Ear infection		Mild	Unlikely	Medication	
	Bi-polar		Moderate	Unlikely	Medication	

	Cramping		Moderate	Unlikely	None	
	Dysfunctional vaginal bleeding		Moderate	Unlikely	None	
	Laparascopic by-pass and cholecystectomy		Moderate	Unlikely	Hospitalization	
	Cholelithiasis		Moderate	Unlikely	Hospitalization	
	Obesity		Moderate	Unlikely	Hospitalization	
	Late period		Mild	Unlikely	Other	Serum pregnancy test-negative
	Migraine		Moderate	Unlikely	Medication	
	Change in Raynards		Mild	Unlikely	None	
	Change in Sjogruns		Mild	Unlikely	None	
	Arthritis		Moderate	Unlikely	Medication	
	Cystitis X 3 over past 12 mths		Moderate	Unlikely	Medication	
	Osteo-arthritis knee and fingers		Moderate	Unlikely	Medication	
(b)(6)	Partial thyroidectomy	(b)(6)	Moderate	Unlikely	Hospitalization	
	Pt kicked in abdomen causing abdominal discom./vag. bleeding		Mild	Unlikely	None	
	Insomnia		Mild	Unlikely	Medication	
	Carpal tunnel release		Moderate	Unlikely	Other	Outpatient surgery
	Cystoscopy		Moderate	Unlikely	Hospitalization	
	Cystitis		Mild	Unlikely	Medication	
	Lumbar pain		Moderate	Unlikely	None	
	Follicular ovarian cyst.		Mild	Unlikely	Medication	
	Periovulation pain		Moderate	Unlikely	Medication	
	Apendicitis		Severe	Unlikely	Other	Apendicectomy laparoscopy.
	Gastric bypass		Moderate	Unlikely	Other	Surgery, weight loss successful-70 lbs.
	Gastric reflux		Mild	Unlikely	Medication	

Diarrea	(b)(6)	Moderate	Unlikely	None	
Osteoarthritis in knees		Moderate	Unlikely	Medication	
Biopsy on lumps on arm and leg		Mild	Unlikely	None	Biopsy (b)(6) showed mastocystitis
Hysteroscopy		Mild	Unlikely	Hospitalization	Insertion of Mirena IUCD
Pelvic pain		Moderate	Unlikely	Hospitalization	Laser surgery to pelvic endometriosis
Urine infection		Mild	Unlikely	Medication	
Abdominal bloating		Moderate	Unlikely	Other	Ultrasound and x-ray
Cervical pain		Moderate	Unlikely	Medication	
Hemorrhoidectomy		Moderate	Unlikely	Other	Surgery, removal of exterior hemorrhoids
Headaches		Moderate	Unlikely	Medication	
Nausea		Moderate	Unlikely	Medication	
Broken right ankle		Moderate	Unlikely	Hospitalization	Plate and 7 screws to ankle
Surgery on torn achilles tendon		Moderate	Unlikely	Other	Day surgery and crutches
Manic episode		Mild	Unlikely	Medication	
Broken ankle		Moderate	Unlikely	Other	Plaster on ankle for 5 weeks.
Fell off balcony		Moderate	Unlikely	Other	Sutures to cut on scalp.
Acute depression		Severe	Unlikely	Hospitalization	
Hysterectomy due to fibroids		Moderate	Unlikely	Hospitalization	
Breast reduction		Moderate	Unlikely	Hospitalization	
Thyroidectomy		Moderate	Unlikely	Medication	
Mirena inserted		Mild	Unlikely	Hospitalization	
Chest infection		Moderate	Unlikely	Medication	
Peri menopausal symptoms		Moderate	Unlikely	Medication	
Back pain		Severe	Unlikely	Medication	

(b)(6)	Thrush	(b)(6)	Mild	Unlikely	Medication	
	Cauter of vulval warts		Mild	Unlikely	Other	Burnt off by GP

Pages 92 through 108 redacted for the following reasons:
- -
(b)(4)-Trade Secret/Confidential Commercial Information
Case Report Form

Conceptus

Dear Study Participant:

Thank you for taking part in the clinical study, "Evaluation of the Safety and Effectiveness of the STOP Device to Prevent Pregnancy in Women Who Are Seeking Permanent Contraception." Your willingness to take part in this study is of great help in the development of the procedure.

Attached is a Participant Questionnaire and Participant Diary for you to complete. This information is a very important part of the clinical study.

The Participant Questionnaire is to be completed one week after the device placement procedure. Please note that these forms are carbon paper and should not be placed on top of each other when writing down your responses. Use a ballpoint pen and press firmly to make sure that your responses can be read on each page of the form. After you have completed the questionnaire, please return it to Helen Plummer in the envelope provided. Helen Plummer will call you in two weeks to discuss your responses to these questions.

Enclosed is a Participant Diary for recording information about your menstrual cycle and sexual activity. Each page of the patient diary can be used for 3 months. Write the names of the months in the top left-hand box next to "Month-", followed by the year. The first month will start with the date your STOP devices were placed. Please check the box that corresponds to the appropriate day(s) of the month that you have your menstrual period or have sexual intercourse. Also indicate any pain experienced during sexual intercourse or during your menstrual period by checking the appropriate box. More specific instructions are found at the bottom of the page on the Participant Diary. An example of what a completed diary might look like is attached.

Please bring your Participant Diary with you when you see Professor Kerin for your 3-month and 6-month visits.

If you wish to speak to someone about the device placement procedure, your recovery, the device itself, how to complete these forms, or any concerns you might have, please call Professor Kerin or Helen Plummer at 8371 3099.

Please remember that it is necessary to use contraception until your device placement has been evaluated and confirmed at the 3-month office visit. At that time Professor Kerin will advise you regarding discontinuing use of contraception.

Please bring this completed form with you to your 3-month visit with Professor Kerin.

Conceptus

Participant Diary

Conceptus Protocol: STOP 07 Safety and Effectiveness of the STOP Device	Pt #: S7- Initials:	Page 1 of 2

Case Report Form #3B: Participant Diary

Month /Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Device Placement																															
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
Pain **																															
Medication ***																															

Month/Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
Pain **																															
Medication ***																															

Month/Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
Pain **																															
Medication ***																															

* Place an "X" in the box that corresponds with the days you have sexual intercourse or have your period.

** If you have pain with sexual intercourse or your period, please put an "M" in the corresponding box if the pain is mild or an "S" in the box if it is severe. If the pain is more than you had **before** the device placement, please put a circle around the "M" or the "S."

*** If you take any medication for pain, please fill out the following information:

Name of Medication	Date Started	# Times Taken per Day	Date Stopped

Please bring this completed form with you to your 6-month visit with Professor Kerin.

Conceptus

Participant Diary

Conceptus Protocol: STOP 07 Safety and Effectiveness of the STOP Device	Pt #: S7- Initials:	Page 2 of 2

Case Report Form #3B: Participant Diary

Month/Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Device Placement																															
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
Pain **																															
Medication ***																															

Month/Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
Pain **																															
Medication ***																															

Month/Year -	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Sexual Intercourse *																															
Pain **																															
Medication ***																															
Contraception Used?																															
Menstruation *																															
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** If you have pain with sexual intercourse or your period, please put an "M" in the corresponding box if the pain is mild or an "S" in the box if it is severe. If the pain is more than you had **before** the device placement, please put a circle around the "M" or the "S."

*** If you take any medication for pain, please fill out the following information:

Name of Medication	Date Started	# Times Taken per Day	Date Stopped

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Case Report Form

P020014/R12/A1

P020014_R012_A001
Essure Permanent Birth Control System

Date: February 7, 2007
Reviewer: Elaine Blyskun, Biomedical Engineer
Division/Branch: DRARD/OBGD

P: P020014_R012_A001
Device Trade Name: Essure Permanent Birth Control System

Company: Conceptus, Inc.
331 E. Evelyn Ave.
Mountain View, CA 94041

Contact: Edward Sinclair
VP, Clinical Research, Regulatory Affairs and Quality Assurance
650-962-4170 (phone)
650-962-5217 (fax)

Background:
The Essure System is intended for use in women who are seeking permanent birth control. It is composed of the micro insert, the delivery system, and the split introducer. FDA approved the PMA on November 4, 2002. The Phase II study was conducted to evaluate long-term safety and effectiveness of this device. Michelle Byrne was originally the lead reviewer for the P020014_R012, the final report of this study. (b)(4)

(b)(4)

Review:

(b)(4)

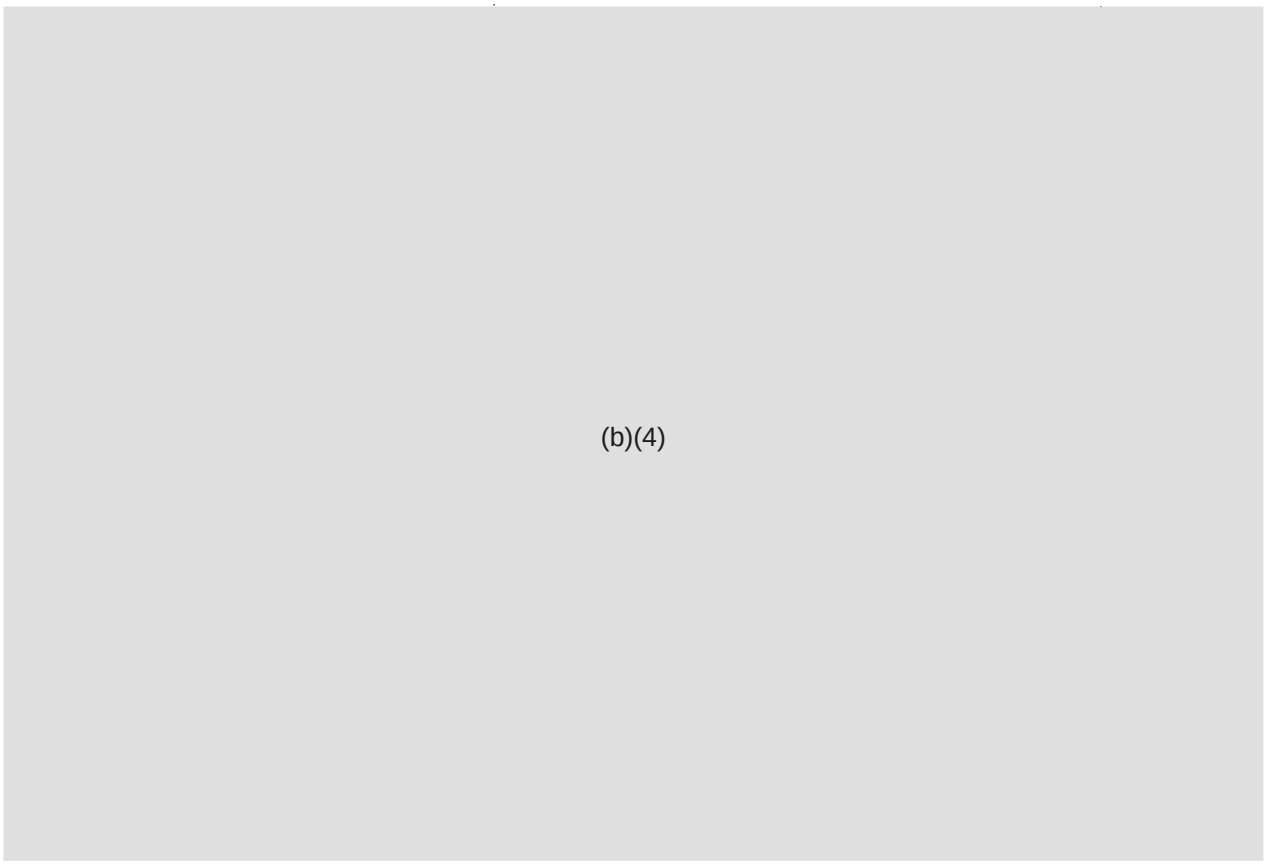
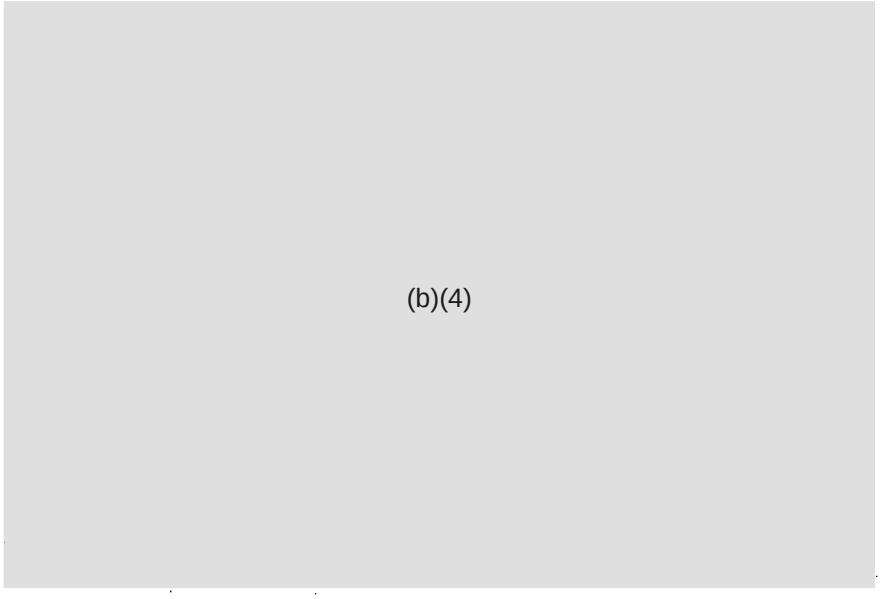
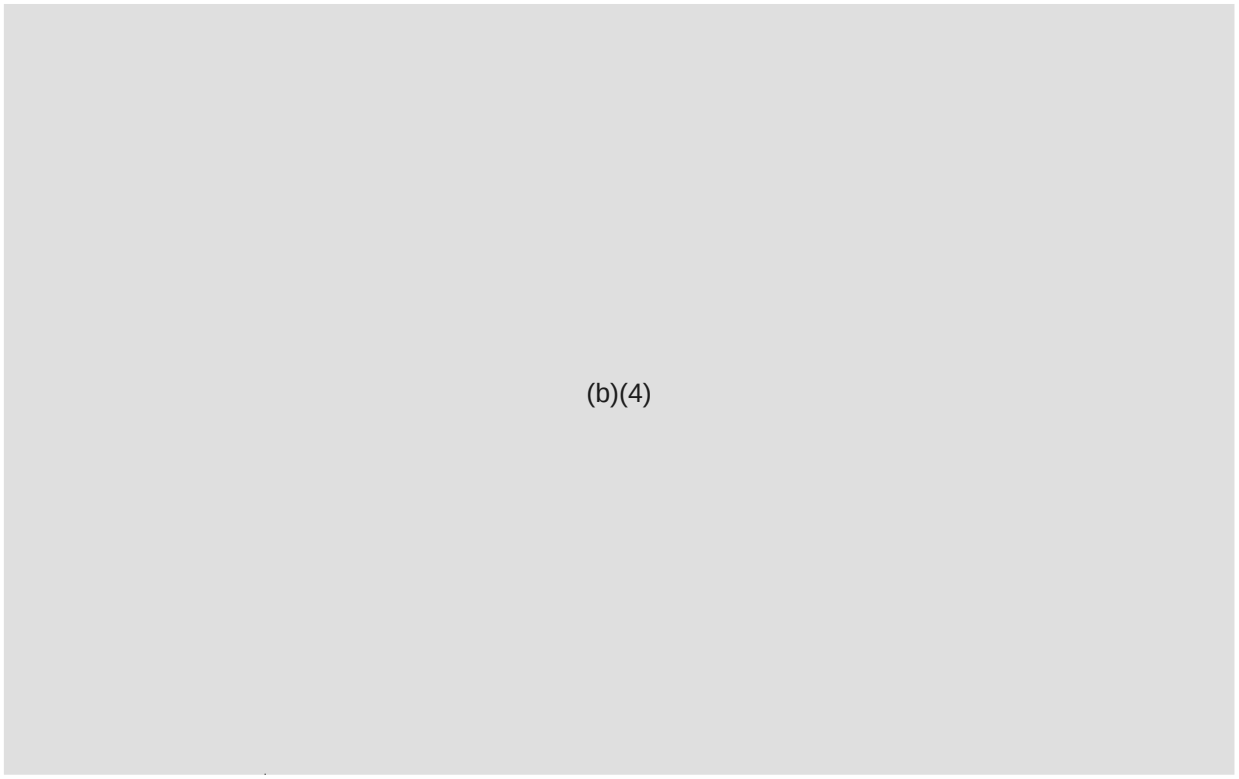
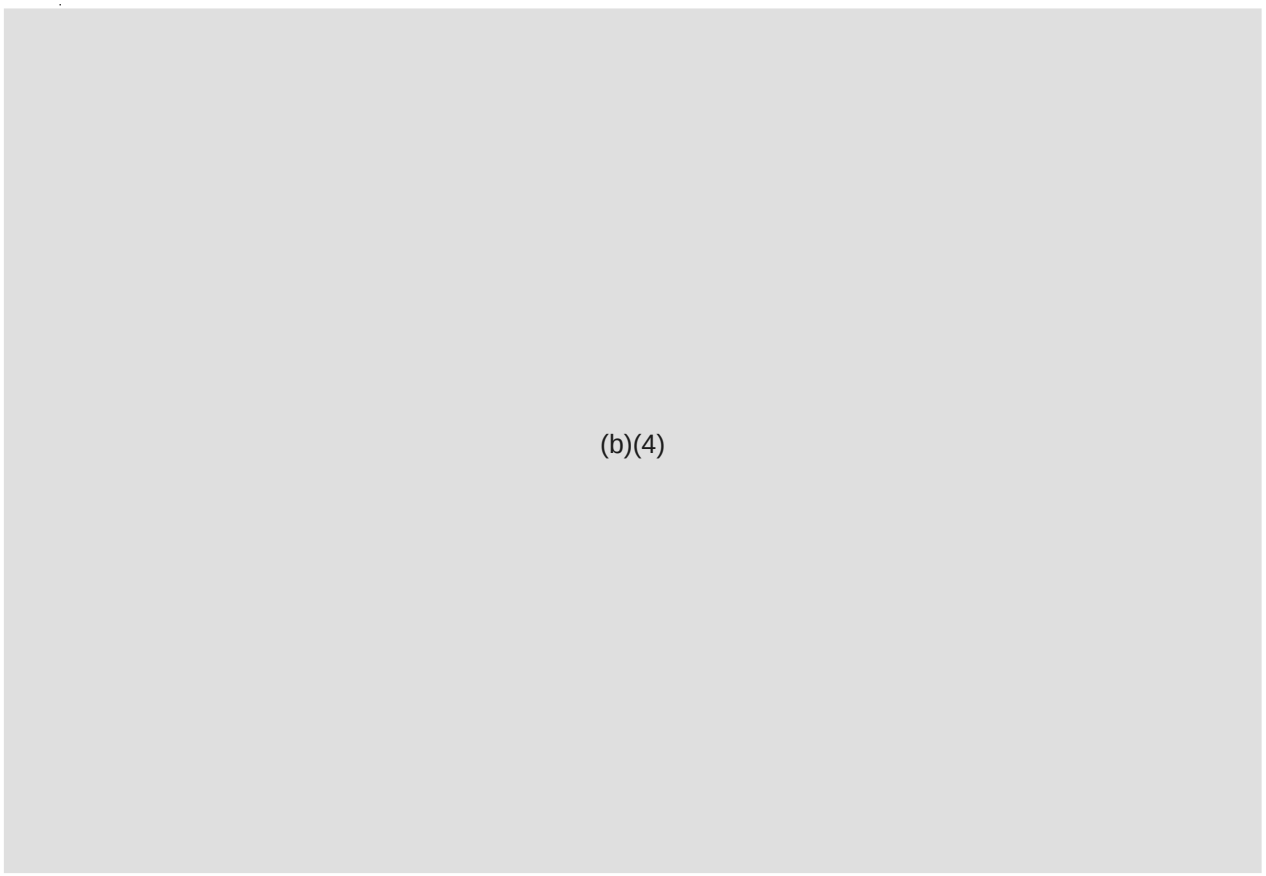


Figure 1.




(b)(4)


(b)(4)

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

Nilsa Loyo-Berrios PhD MS has reviewed this information. Her review, dated January 31, 2007, has the following conclusions/recommendations:

(b)(4)

2. Review of P020014/R012 is completed.

3. Information on pain severity by type of anesthesia could be useful for physicians and patients.

Dr. Corrado has also reviewed this information. She indicates in her email review, dated February 5, 2007, that (b)(4). She does not have any additional questions for the sponsor.

Recommendation:

(b)(4) We will send the sponsor a letter to acknowledge that this post approval study is complete.

Elaine Blyskun Date: February 7, 2007

Colin Pollard, Chief, OGDB Date 2/12/07

/ / Concur

/ / Do Not Concur

Memorandum

Date: January 31, 2007

From: Nilsa Loyo-Berríos, PhD, MS, Epidemiology Branch (EB)
Division of Post Market Surveillance (DPS)
Office of Surveillance and Biometrics (OSB), HFZ-541

Subject: Epidemiologic Review of the Amendment to PMA P020014/R012, Essure ™ System

To: Elaine Blyskun, Obstetrics and Gynecology Devices Branch, DRARD/ ODE, HFZ-470

Through: Danica Marinac-Dabic, MD, PhD, Chief, EB, DPS/OSB, HFZ-541 _____
Thomas P. Gross, MD, MPH, Director, DPS, OSB, HFZ-520 _____

Purpose

The purpose of this memorandum is to present the epidemiologic review of Amendment 001 to the Final Report for the Phase II Study (P020014/R012). The study was conducted to evaluate long-term safety and effectiveness of Conceptus Essure ™ System for permanent birth control.

Background

The final results for the Phase II study were included in P020014/R012. (b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

2. Review of P020014/R012 is completed.

3. Information on pain severity by type of anesthesia could be useful for physicians and patients.

Nilsa I. Loyo-Berríos, PhD, MS

cc: Julia Corrado, HFZ-470
Colin Pollard, HFZ-470
Diane E. Dwyer, HFZ-520

Document History:
Drafted: NLoyo-Berríos, December 7, 2006
Reviewed: DMarinac-Dabic, January 31, 2007

Blyskun, Elaine

From: Corrado, Julia A
Sent: Monday, February 05, 2007 3:36 PM
To: Blyskun, Elaine
Cc: Pollard, Colin M.
Subject: FW: P020014_R012 and P020014_R013 Responses

Attachments: Essure ThermaChoice responses P020014_R013_A001.doc; Essure Review Amendment 1 for Phase II Final Report (R012).doc

February 5, 2007

Elaine,

I have read Nilsa's excellent reviews, and don't believe we need to follow up with the sponsor. Nilsa's main suggestions (and my comments) follow:

(b)(4)

Thanks,

Julia

2.

From: Blyskun, Elaine
Sent: Monday, February 05, 2007 1:48 PM
To: Corrado, Julia A
Subject: P020014_R012 and P020014_R013 Responses

Julia,
When you get a chance, would you please look over Nilsa's reviews of P020014_R013_A001 (Essure/Thermachoice study report) and of P020014_R012_A001 (Phase II Clinical Study final report)?

P020014 R14 A1 C1

P020014/R14/A1 C1

Conceptus®

P-13

November 30, 2006

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

Re: **Amendment #1 to the Phase II Clinical Study Final Report**
PMA P020014, Conceptus Essure® System for Permanent Birth Control

Dear Ms. Byrne,

This Amendment to the Phase II Clinical Study Final Report is being submitted in response to questions received from the Agency on August 14, 2006. (b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

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

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

Please let me know if you have any questions or need additional information. I can be reached by phone at (650) 962-4170, by fax at (650) 691-4729, or by email at esinclair@conceptus.com. Please note the new address and contact information below.

Sincerely,

Edward J. Sinclair
Vice President, Clinical Research, Regulatory Affairs and Quality Assurance
Conceptus, Inc.
331 E. Evelyn Ave.
Mountain View, CA 94041 USA
Direct: (650) 962-4170
Fax: (650) 691-4729

Exhibits: 1

EXHIBIT 1

Phase II Clinical Study Final Report
AMENDED

Pain during the Micro-insert placement procedure was reported by (b)(4) women who underwent a placement procedure (first and second procedures combined). Pain during Micro-insert placement was rated as less than or equal to that expected in (b)(4) women and greater than expected in (b)(4) (b)(4) women. The remaining (b)(4) women answered "n/a" to this question because placement was not achieved (b)(4) the woman received general anesthesia for the placement procedure (b)(4) woman had IV sedation (b)(4) For unknown reasons (b)(4) women chose not to answer the question.

Adverse events

A total of (b)(4) women (b)(4) experienced an adverse event on the day of the procedure (b)(4) women had vaso-vagal responses that were treated with atropine, (b)(6) resolved immediately and (b)(6) required observation for several hours prior to discharge. One woman (b)(6) complained of severe leg pain during the procedure that was likely due to positioning. The pain was resolved within 2 hours with analgesics and a change in position.

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One woman (b)(6) complained of severe post-op pain. This may have been related to Micro-insert deployment in the fallopian tube. The pain resolved with analgesics within 8 hours following the procedure.

In (b)(4) women (b)(6) the proximal band of the Micro-insert became detached during Micro-insert placement and was noted on the x-ray to be located in the uterus. There were no sequelae and all women passed the band with subsequent menses. A thorough evaluation of this technical failure revealed that unsatisfactory variability existed in the manufacturing process of attaching the proximal band to the Micro-insert. This manufacturing process was revised and a new inspection and release test method was established to address this issue.

One-week Questionnaire

One week after Micro-insert placement, women were asked to complete a questionnaire, rating their tolerance of the Micro-insert placement procedure and noting any pain, bleeding or unusual symptoms that may have occurred in the intervening seven days. Two weeks post-Micro-insert placement, women were contacted to assess any adverse events and encourage completion of the patient questionnaire. Patient questionnaires from (b)(4) of 227 women undergoing Micro-insert placement were received. The remaining (b)(4) did not complete the questionnaire because they were either a bilateral failure (b)(4) or a unilateral failure (b)(4)

Tolerance of Procedure

Of the (b)(4) women who completed the one-week questionnaire, tolerance of the Micro-insert placement procedure was rated as "good" to "excellent" in (b)(4) women (b)(4) fair in (b)(4) women (b)(4) and poor in (b)(4) women (b)(4) (b)(4)