PO20014 R8

SEP - 2 2005

Mr Edward Sinclair
Vice President, Clinical Research and Regulatory Affairs
Conceptus, Inc
1021 Howard Avenue
SAN CARLOS CA 94070-4700

Re P020014/R8
Essure® System for Permanent Birth Control
Received March 16, 2005
Amended July 5, 2005

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(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related"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

Based on the findings of the study, please submit a PMA supplement that addresses the following labeling concerns

- Updated Physician and Patient Labeling to include results of the postapproval study Labeling should include information on the number of patients excluded and why these patients were excluded from the postapproval study

PMA supplements should be submitted in 3 copies and should include the FDA reference number for this PMA Please submit your PMA supplement to the following address

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 letter, please contact Michael Bailey, Ph D at (301) 594-1180

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-401 (Document Mail Center)
HFZ-402 (PMA Staff)
HFZ-470 (DRARD)
D O
HFZ-550 (OSB/DBS)
HFZ-541 (OSB/DPS)

Drafted 8/29/05 MTB
Final 8/31/05

FILE COPY

OFFICE	SURNAME	DATE		OFFICE	SURNAME	DATE		OFFICE	SURNAME	DATE
HFZ-470	Bailey	8/31/05		Z-470	Drogdon	9-1-05				
HFZ 470	Curtis	8/31/05								
HFZ 470	Vinson for Pollard	8/31/05								

U.S GPO 1986-169-089

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP - 2 2005

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Vice President, Clinical Research and Regulatory Affairs
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(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related"

P020014 R8 C1

P020014/RS/C
Supplement to PMA P020014

Conceptus®

March 15, 2005

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

RE: (b)(4)

P020014, Conceptus Essure® System for Permanent Birth Control

To Whom it May Concern,

In accordance with 21 CFR 814.39(a), Conceptus is submitting the enclosed PMA supplement for modification of the Essure placement rate labeling and

Background

The Food and Drug Administration granted Pre-Market Approval (P020014) to the Conceptus Essure System on November 4, 2002. In the approval letter, Conceptus agreed to provide data on a post approval study in the U.S. with newly trained physicians in post approval reports. This study was intended to document the bilateral placement rate for newly trained physicians (800 patients, 40 physicians, first 20 attempts). These data were intended to evaluate the training procedures and to update labeling. Data collection included 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.

Interim Study Results - Essure Placement Rate

(b)(4)

(b)(4)

(b)(4)

(b)(4)

Labeling Changes

(b)(4)

B. Patient Labeling

(b)(4)

Exhibits

1. Clinical Data Report: Post Approval Study for Newly Trained Physicians
2. Placement Rate Summary: Post Approval Study for Newly Trained Physicians
3. Physician Labeling Changes
   The *Essure Instructions for Use* showing text modifications related to the Post Approval Study and Essure placement rates.
4. Patient Labeling Changes
   The *Essure Patient Information Booklet* showing text modifications related to the Post Approval Study and Essure placement rates.

The information contained in this PMA supplement is considered confidential and Conceptus therefore requests protection of this information in accordance with 18 USC 1905, 21 USC 331(I), 5 USC 552.

Please let me know if you have any questions or need additional information. I can be reached by phone at (650) 628-4790, by fax at (650) 802-2890, or by email at esinclair@conceptus.com.

Sincerely,

Edward J. Sinclair
Vice President, Clinical Research, Regulatory Affairs and Quality Assurance
Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070 USA
(650) 628-4700

Exhibits: 1-4

Exhibit 1

Clinical Data Report: Post Approval Study for Newly Trained Physicians

Conceptus®

CLINICAL DATA REPORT: POST APPROVAL STUDY

for Newly Trained Physicians

Data current to January 24, 2005

Table of Contents

Exhibits

Table of Contents (Cont'd)

Tables

Clinical Data Report: Post Approval Study for Newly Trained Physicians

A. Background

This report contains data obtained from the U.S. Post-Approval Study for Newly Trained Physicians as part of the post-approval requirements for the Essure PMA No. P020014 (approval granted by FDA on November 4, 2002).

The data in this report are current to January 24, 2005.

B. Study Purpose and Protocol

Purpose

According to the post-approval requirements, this study is intended to document the bilateral placement rate for newly trained physicians. These data will be used to evaluate the training procedures and to update labeling. Data collected will 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.

Study Design

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

Although only 40 physicians are needed to reach a total of 800 women (b)(4) physicians will be enrolled in this study in the event that not all physicians complete a total of 20 cases, or do so on a timely basis. Enrollment in this study will cease after data is available from 40 physicians who have provided data regarding 20 cases of Essure placement attempt.

(b)(4)

(b)(4)

study. Such physicians will be enrolled in the study only if: 1) they agree to participate,

and 2) they do not have previous experience in Essure micro-insert placement. In addition, they will not contribute cases to this study until after they have completed the preceptoring portion of the training program.

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

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.

Primary Endpoints

The primary endpoints are as follows:

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

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

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

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

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

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

Placement Device

The study was initiated after approval of PMA P020014 using the Essure "gamma" delivery device. Subsequently, design modifications to the delivery catheter were submitted to FDA as PMA supplement P020014/S1. Approval of the "coil catheter" design occurred on March 6, 2003. The coil catheter design was introduced into the post-approval study soon after approval.

Placement Procedure

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

Follow-up Procedures

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

Study Dates

The Essure System was placed into the first Post Approval Study patient on February 10, 2003. (b)(4)

(b)(4)

C. Inclusion and Exclusion Criteria

Study participants were women who were seeking permanent contraception. All inclusion and exclusion criteria from the Instructions for Use approved under the PMA were used.

Additional inclusion criteria:

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

D. Study Site Information

A total of physicians at (b)(4) US sites have initiated Essure placement procedures as part of the Post Approval Study. A total of (b)(4) women have been enrolled in the study as shown in ***Table 1*** below.

Table 1. Number of Women Enrolled per Investigator

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

On average, the (b)(4) investigators performed (b)(4) Std. Dev.) Essure placement procedures with a range from (b)(4) A total of (b)(4) investigators have performed (b)(4) more procedures. The median number of Essure procedures per investigator was (b)(4) A complete list of physician names and study site addresses are provided in ***Exhibit A***.

According to the Study Protocol, no more than (b)(4) in ***Table 2***.

Table 2. Procedure Setting

Facility Category	Number of Facilities	Percent of Total (N= (b)(4)
(b)(4)		

The type of facility where the Essure procedure was performed and the number of procedures attempted at each location is summarized in ***Table 3***, below.

Table 3. Type of Facilities placing Essure

Type of Facility	Number of Procedures	Percent of Total
(b)(4)		

E. Physician Experience

Prior to performing Essure placement procedures, each participating investigator was asked to provide information regarding their prior gynecological procedure experience.

(b)(4)

(b)(4)

F. Study Demographics

As of January 24, 2005 a total of (b)(4) women have been enrolled into the Post Approval Study. (b)(4)

(b)(4)

(b)(4)

Demographic information of the study subjects is provided in the ***Tables 5 - 8*** below.

Table 5. Ethnic Distribution

Ethnicity	Number	Percent of Total
Non-Hispanic or Latino	(b)(4)	
Hispanic or Latino		
Total		

Table 6. Race Distribution

Race	Number	Percent of Total
White / Caucasian	(b)(4)	
African-American or Black		
Hispanic		
Asian		
Indian		
White/Caucasian and Hispanic		
White/Caucasian and African-American or Black		
American Indian or Alaska Native		
No Answer / Unknown		
Total		

Table 7. Highest Level of Education

Education Level	Number	Percent of Total
5	(b)(4)	
6		
7		
8		
9		
10		
11		
High School		
13		
Community College		
14		
College		
Post Graduate		
Trade/Vocational School		
Declined to state		
No answer provided		
Total		

Table 8. Annual Household Income

Annual Household Income	Number	Percent of Total
< $25,000	(b)(4)	
$25,000 - $50,000		
$50,000 - $75,000		
> $75,000		
Declined to state		
No answer provided		
Total		

The average age of the women undergoing device placement was (b)(4) (b)(4) years. ***Table 9*** below provides the age distribution. Other physical and medical history demographics are listed in ***Table 10***.

Table 9. Age Distribution at time of Essure placement

(b)(4)

Age	Number	Percent of Total
	(b)(4)	

Table 10. Patient Demographics

Variable	N*	Mean	Median	Range	Std deviation
Age	(b)(4)				
Height					
Weight					
Body Mass Index					
Gravidity					
Parity					

* Some data fields were left blank for some women

Prior Abdominal Surgery

(b)(4)

Prior Inflammatory Conditions and STD History

(b)(4)

Table 11. Prior Inflammatory Conditions and STD History

Yes	(b)(4)
No	
Not Answered	
Totals	

Primary Method of Contraception Used

(b)(4)

Table 12. Primary Contraceptive Method

Primary method of contraception prior to Essure procedure	Number of Women	Percent of Total (b)(4)
(b)(4)		

G. Pre-Procedure Data

(b)(4)

Table 13. Use of pre-procedure hormones for endometrial manipulation

Hormones prescribed pre-procedure?	Number of Procedures	Percent of Total
(b)(4)		

Table 14. Type of pre-procedure hormones prescribed

Type of hormonal manipulation	Number of Procedures	Percent of Total
(b)(4)		

The use of pre-procedure non-steroidal anti-inflammatory drugs (NSAIDs) is recommended by the Essure instructions for use. ***Table 15*** below, shows the number of patients that were prescribed NSAIDs prior to the placement procedure.

Table 15. Use of pre-procedure NSAIDs

NSAIDs prescribed pre-procedure?	Number of Procedures	Percent of Total
(b)(4)		

H. Anesthesia

(b)(4)

Table 16. Predominant Anesthesia Used

Predominant Anesthesia	Number of Procedures	Percent of Total
(b)(4)		

I. Study Devices: Essure System Designs (Catalog Numbers)

The Post Approval Study for Newly Trained Physicians was initiated after approval of the original PMA (P020014) in November 2002. Essure Systems with the (b)(4) version of delivery catheter (Catalog No. ESS005) were distributed to physicians for use in the Study. A new "coil" version of delivery catheter (Catalog No. ESS205) was developed and approved according to P020014/S1 in March 2003. (b)(4)

(b)(4)

(b)(4)

J. Hysteroscope Data

(b)(4)

Table 17. Brand of Hysteroscope Used

Hysteroscope Brand	Number of Procedures	Percent of Total (N=514)
(b)(4)		

Table 18. Diameter of Hysteroscope Sheath

Hysteroscope Diameter (mm)	Number of Procedures	Percent of Total (N=514)
(b)(4)		

J. Micro-insert Placement Data

Figure 1 below shows the flow of outcomes in the post-approval study. The following sections describe these outcomes in more detail.

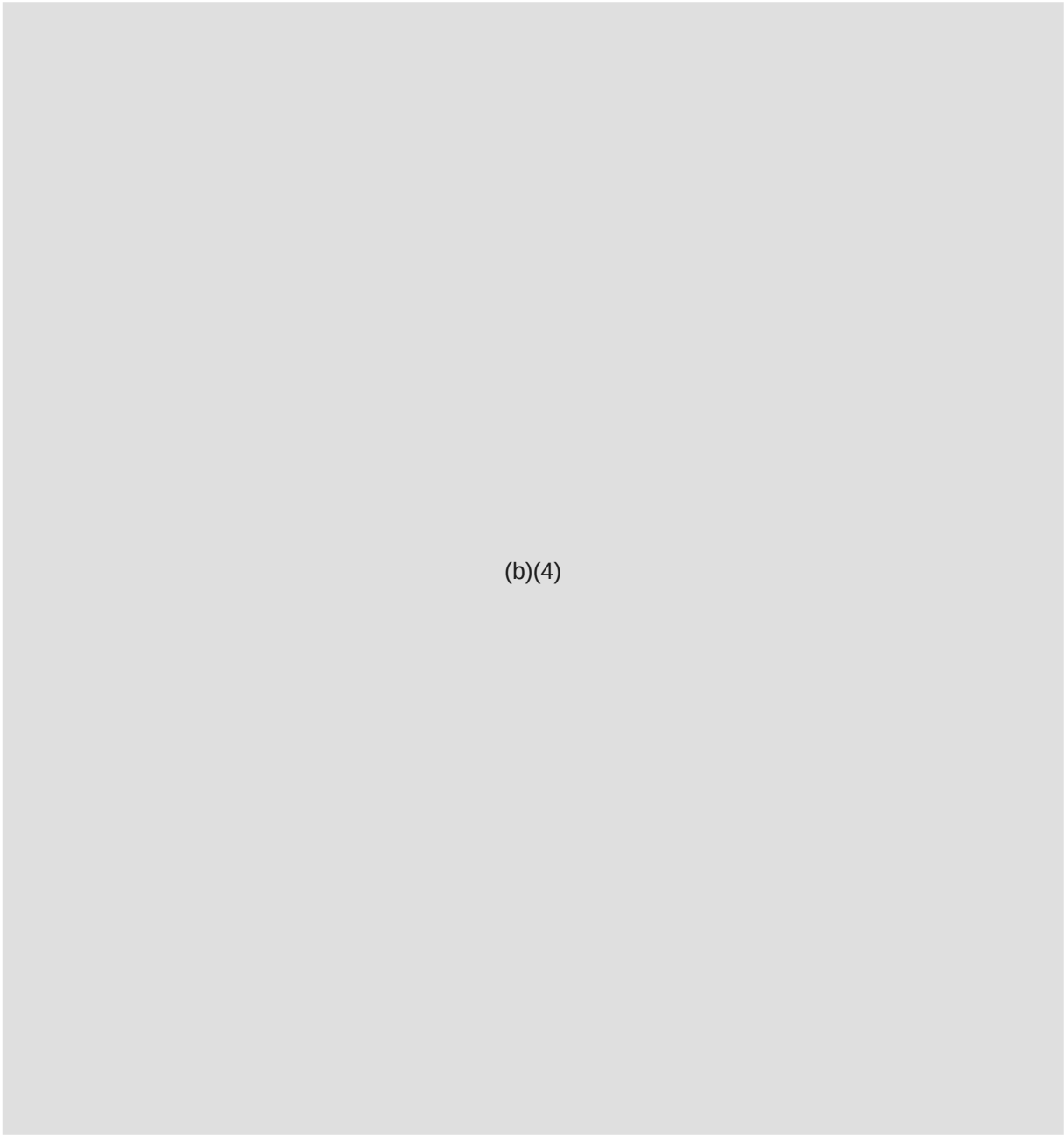

Figure 1. Patient "outcome flow" in the Post Approval Study for Newly Trained Physicians

Hysteroscopic Procedure Time

(b)(4)

Table 20. Primary cause of increased procedure time

Primary Cause	Examples	Number of procedures
(b)(4)		

Procedure "Non-Attempts"

(b)(4)

Table 21. Placement Procedure Non-Attempts

Patient No.	Reason for non-attempt of placement procedure
	(b)(4), (b)(6)

Unilateral Placement - Intentional

(b)(4)

Table 22. Intentional Unilateral Placement Attempt: Basis of protocol violation

Patient No.	Description
(b)(4), (b)(6)	

Placement Failure

(b)(4)

Table 23. Categorization of Placement Failures

Primary reason for placement failure	No. of Patients	Percent of total (b)(4)	Patient No.
(b)(4), (b)(6)			

Table 24. Causes of Unilateral Placement Failure

Pt. #	Micro-insert Placement		Description
	Left	Right	
			(b)(4), (b)(6)

Table 25. Causes of Bilateral Placement Failure

Patient No.	Bilateral Failure Description
	(b)(4), (b)(6)

Placement Rates - Combined

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

Micro-insert placement rates are listed in ***Tables 26-29***.

Table 26. Placement Rates - all patients included (b)(4)

Placement Status	Number	Percent
(b)(4)		

Table 27. Placement Rates - excluding contraindicated patients

Placement Status	Number	Percent
(b)(4)		

Table 28. Placement Rates - excluding contraindicated patients & non-attempts

Placement Status	Number	Percent
(b)(4)		

Table 29. Placement Rates - excluding all confounding

Placement Status	Number	Percent
(b)(4)		

Placement Rates - Gamma vs. Coil Catheter Designs

(b)(4)

Table 30. (b)(4)

Placement Status using Gamma Catheter	Number	Percent
(b)(4)		

Table 31. Micro-insert Placement Rate for Coil Catheter Design (ESS205)

(b)(4)

Placement Status using Coil Catheter	Number	Percent
(b)(4)		

Table 32. Micro-insert Placement Rate for Coil Catheter Design (ESS205)

(b)(4)

Placement Status using Coil Catheter	Number	Percent
(b)(4)		

Trailing Lengths

(b)(4)

Device Issues and Malfunctions

(b)(4)

(b)(4)

Table 34. Device Issues and Malfunctions

Patient No.	Model	Lot	Description
(b)(6)	ESS005	(b)(6)	Device did not deploy on the right had to use second device. Malfunction may have been secondary to forward pressure on device and angulation of catheter. Tubal spasm was present.
	ESS005		2 attempts at right placement as, when deploying device, it came out of tube on first attempt. Difficulty disconnecting device from delivery system on right with some separation of dacron fiber from coil
	ESS205		First device deployed but did not release-came out
	ESS005		Left placement x3 due to non-release of device
	ESS005		Difficult release with micro-insert
	ESS005		Essure device tip damaged with introduction into hysteroscope
	ESS005		Spontaneous detachment of micro-insert up into right tube/ostium. Second device placed without incident
	ESS005		Three Essure devices used until successful insertion (tubal spasm caused bent tips)
	ESS005		The first device, placed well, mis-fired and remained attached to the delivery catheter and did not release. Second device bent.
	ESS205		Initially placed device into right tube could not be detached from cable and required removal and placement of a second device (successful)
	ESS205		Again difficulty with release of the cable from the micro-insert after deployment. However, with several minutes of revolutions, cable did separate and bilateral placement achieved.

Table 34. Device Issues and Malfunctions (Cont'd)

	ESS205		Two devices failed. One failed to release delivery wire and second tip became unraveled after insertion into tubal ostium before deployment: both from same Lot.
	ESS205		The first Essure tip was bent as it was placed through the hysteroscope and it was discarded
	ESS005		One implant not used because tip was bent in insertion attempt on the left tube. Left tube had a lateral orientation
	ESS005		Right ~ 2 devices would not release
	ESS205		Left ~ Failure to deploy/release
	ESS205		Left tube Essure did not release and was withdrawn New implant inserted without difficulty.
	ESS005		Guide wire would not detach. Inner sleeve detached and had to be manually removed. Trailing coils distorted secondary to difficulty removing wire
(b)(6)	ESS205	(b)(6)	Manufacturing difficulties in Essure catheter, Thumb wheel did not go back easily on right side catheter, and post detachment difficulties
	ESS205		Difficulty moving thumb wheel back, which may have had detachment difficulty of coil on right side
	ESS205		Detachment difficulty with right Essure catheter, 15 coils exposed in right tube
	ESS205		Detachment difficulty
	ESS205		Thumbwheel stuck on one catheter, some detachment difficulty
	ESS205		Left (b)(6) Original intro catheter failed to retract. Device from same lot successfully placed.
	ESS205		Catheter was placed in the right tube and would not release. Pulled right out, needed new catheter which was placed without difficulty
	ESS205		Device seemed to release too easily today. I felt like counter clockwise rotation was not required to release the catheters
	ESS205		Tip bent, needed to open and use another catheter

(b)(4)

below. One physician reported that a hysteroscope was not adequately cleaned prior to the Essure placement procedure and two other reports indicate a perceived proximal movement of the micro-insert, possibly due to tubal spasm immediately after placement. Lastly, one patient receiving IV sedation was moving too much during the procedure

because she was coughing. She was converted to general anesthesia to reduce her movement so the placement procedure could proceed.

Table 35. Miscellaneous Physician Comments

Patient No.	Description
(b)(4), (b)(6)	

Table 35. Miscellaneous Physician Comments (Cont'd)

(b)(6)	Patient was initially placed under IV sedation and a paracervical block was placed. After adequate anesthesia, the 5-mm hysteroscope was inserted into the uterine cavity. She began coughing and bucking several times during the procedure, therefore converted to a general anesthetic (to prevent her from moving too much and interfering with the Essure placement procedure). Once the patient was comfortable, (b)(6) then proceeded with the Essure placement procedure. After the procedure, the patient was moved to the supine position in stable condition, awakened, and transferred to the recovery room.

K. Safety of Micro-insert Placement Procedure

Adverse Events

Adverse events that occurred during and after the Essure placement procedure have been reported in (b)(4) women (b)(4) . All reported events were minor with the exception of Patient (b)(6) . One micro-insert perforated the left uterine fundus and embedded in omentum causing pain. The peritoneal portion of the micro-insert was laparo-scopically removed and each tube was banded with Falope rings. The patient reported increased pain of unknown etiology and was to be scheduled for diagnostic studies and became lost to follow-up. None of these events represent unanticipated adverse device effects. ***Table 36*** summarizes all events and the patient management for each.

Table 36. Adverse Events

Patient No.	Adverse Event / Complication
(b)(6)	Physician performed endometrial ablation using rollerball immediately following Essure placement. He hit one of the micro-inserts with the rollerball and fractured the micro-insert. Because the physician was uncertain as to the future effect on the Essure placement, he proceeded to perform bilateral tubal ligation. There was no patient injury.
	Patient has a Transposition of the Great Vessels and on waking up had a temporary decrease in pulse; her blood pressure remained stable and patient had no sequelae from this transient event
	Bleeding was seen at the tenaculum site on the cervix that required suturing.
	The patient developed elevated blood pressure post-Essure placement procedure and was given intravenous Apresoline. This was not related to the procedure (according to the physician) and the patient was discharged the same day. This patient underwent concomitant Hydrothermal (HTA) endometrial ablation immediately before the Essure placement procedure.

Table 26. Adverse Events (Cont'd)

	The patient became light-headed and diaphoretic. She was observed for one hour; improved; released feeling fine.
(b)(6)	According to (b)(6) medical file, the patient is a (b)(6) year -old grava 2, para 1 with 1 ectopic who had a Novasure endometrial ablation followed by Essure hysteroscopic sterilization procedure on (b)(6) At the time of her initial procedure, the tubal ostia were marked with methylene blue. The Novasure ablation was then performed followed by placement of the Essure tubal sterilization micro-inserts, which were placed without difficulty. Postoperatively, she developed abdominal pain, and was subsequently readmitted and underwent laparoscopy by (b)(6). At the time of operation, she was noted to have a liver and stomach normal in appearance. The uterus was anteverted and normal in appearance. The overies were normal in appearance. The right fallopian tube appeared to have an implant with proximal stiffening and the distal fallopian tube was normal. The left fallopian tube appeared normal, and there were Essure micro-insert coils protruding from the left posterior uterine fundus and embedded in omentum. Traction was placed on the Essure coils to remove the omental portion of the device, and the uterine portion of the device was grasped and removed. According to (b)(6), these areas were surprisingly hemostatic. A small portion of the Essure device could not be located in the omentum. There was excellent hemostasis and the fallopian tubes were banded with a Falope ring, which was placed on each tube. The patient reportedly did well with some cramping and continued postoperative pain; however, had markedly increased pain as of (b)(6) and reported for an office visit with (b)(6) on (b)(6). She has apparently been taking ibuprofen and Percocet. She states that she continues to have flatus and have bowel movements. She denies any abdominal distention, nausea or vomiting. She denies any vaginal bleeding. Impression: Postoperative abdominal pain. Etiology unclear at this time but will admit for diagnostic studies. Possibilities would include bowel injury, tubal spasm secondary to Falope rings, endometritis, urinary tract infection, or possible omentum adhesions to the Falope ring site. (b)(6) has been unable to locate the patient for follow-up. Letters addressed to her home and have been returned to the office with no forwarding address.
	Uterine perforation by hysteroscope during procedure due to cervical stenosis. Essure procedure not performed due to physician's inability to get the hysteroscope into the uterus. Perforation not related to Essure device. No additional procedures were performed.

Table 26. Adverse Events (Cont'd)

	The tubes were too lateral, and the fluid deficit was too great to continue. Laparoscopy failed to show the location of the excess fluid (1800cc), but the patient did well. No Essure devices were placed and the patient underwent bilateral tubal occlusion with banding. The patient was monitored in recovery for about 4 hours, her electrolytes were checked and she did not show any untoward effects and was able to go home that evening. The physician worked along with the anesthesiologist to assess her fluids, and the anesthesiologist agreed that she was stable. She was given a dose of Lasix 10mg IV, and she put out a good amount of urine as a result. Her lung exam, vital signs, and pulse oximetry readings were all normal.
	Patient reported mild cramping post-procedure. Tylenol was given. Patient reported no pain at discharge.
(b)(6)	Patient reported persistent pelvic pain/pressure beginning several days after the Essure placement procedure on (b)(6) On (b)(6) a total hysterectomy was performed. Findings were normal. Patient had a history of interstitial cystitis and subsequently diagnosed with bladder cancer.
	Patient complaint of uterine cramping. Demerol 50mg, and Toradol 30mg given IV in post op recovery room
	Patient reported feeling crampy during the Essure placement procedure.
	One device placed lateral to right tube. Next device placed correctly in right tube. The physician stated that the first device did not perforate completely through the uterus. The micro-insert was in the side wall of the uterus and the physician decided not to attempt to remove it. As of (b)(6) the physician is still waiting for the patient to undergo HSG to see if the misplaced device is still even in the uterus. The patient has remained asymptomatic since the placement procedure.

L. Concomitant Procedures

Additional information was collected during the course of the Post Approval Study to determine the types of concomitant procedures performed at the discretion of the participating physicians. They were also asked if the additional procedures had any impact on the Essure procedure/device. A total of (b)(4) patients underwent

(b)(4)

Table 37. Concomitant Procedures

Concomitant Procedure	Performed Before Essure Placement	Performed After Essure Placement	Total number of this type of procedure
(b)(4)			

(b)(4)

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

Table 38. Concomitant Procedure Effects

Did the concomitant procedure(s) have an impact on the Essure procedure?	Number of Women	Percent of total with concomitant procedures (N=86)
(b)(4)		

M. Clinical Trial Conduct

(b)(4)

The Post Approval Study protocol and samples of the electronic case report forms were previously submitted in the PMA Amendment dated October 17, 2002 (Volume 1 of 1). A reference copy is included in this report in ***Exhibit G***.

N. Study Deviations

Deviations to the study protocol included a few minor deviations such as late signatures on the informed consent (there is a very brief consent statement in the Protocol primarily to comply with HIPAA regulations).

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

EXHIBIT A: POST APPROVAL STUDY SITES AND PHYSICIANS

Exhibit A. Post Approval Study Sites and Participating Physicians

The table below lists each enrolling site/physician participating in the Post Approval Study.

Site #	Physician Name	Site Address	Academic or Community	Training Sign Off Date
(b)(4), (b)(6)				

Exhibit A. Post Approval Study Sites and Participating Physicians (Cont'd)

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

EXHIBIT B: PROCEDURES REQUIRING ADDITIONAL HYSTEROSCOPY TIME

Exhibit B. Procedures requiring additional hysteroscopy time

Patient ID	Procedure Time (min)	Explanation for additional procedure time
(b)(4), (b)(6)	35	Additional or alternate equipment used to accomplish both Essure and Rollerball endometrial ablation
	56	Had to change to cautery loop to remove a polyp that was interfering with ostial visualization
	39	Device did not deploy on the right and had to use second device. Malfunction may have been secondary to forward pressure on device and angulation of catheter. Tubal spasm was present.
	22	2 attempts at right placement as, when deploying device, it came out of tube on first attempt. Difficulty disconnecting device from delivery system on right with some separation of dacron fiber from coil
	29	Difficulty with obtaining good visualization secondary to distension as well as fluffy endometrium on left obscuring view. Tissue removed with grasper. First device deployed-did not release-came out
	34	Patient on Depo-Provera with bilateral veiled ostia. Grasper used to identify bilaterally. Difficult distension secondary to patulace cervix and fluffy endometrial lining.
	20	Polyp obstructing view was removed with grasper in piecemeal
	18	Fibroid/Polyp removal
	35	Patient with dilated cervix which necessitated use of 2 tenaculi as well as ring forceps
	50	Poor distension and endometrium prevented proper visualization of both ostia
	44	Left ostium not visualized and obstruction/spasm of right tube
	59	Left placement x3 due to non-release of device
	28	Difficult release with spring
	27	Right ostium not visualized. Tubal obstruction/spasm of left tube. Fallopian tubes appeared horizontal (concurred laparoscopically)
	28	Tubal obstruction/spasm of right tube
	54	Unable to visualize right tubal ostium due to tubal obstruction, confirmed at laparoscopy with no dye passage through tube.
	35	Tubal obstruction/spasm of right tube. Tubal ostia located laterally, preventing placement in the right tube
	31	Tubal obstruction/spasm of both tubes. Tubal ostia located laterally, preventing placement in both tubes
	25	Polyp removal
	29	Very lateral tubes. We had a problem with the distension and fogging of the hysteroscope requiring removal of the hysteroscope to "de-fog" it and replace between the right and left tube.

Exhibit B. Procedures requiring additional hysteroscopy time (Cont'd)

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

Exhibit B. Procedures requiring additional hysteroscopy time (Cont'd)

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

Exhibit B. Procedures requiring additional hysteroscopy time (Cont'd)

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

EXHIBIT C: CONCOMITANT PROCEDURES

Exhibit C. Concomitant Procedure Data

Patient No.	Procedures performed in conjunction with the Essure procedure	Performed BEFORE or AFTER Essure placement?	Did any additional procedure have an impact on the Essure procedure?
(b)(4), (b)(6)	Rollerball EA	After	No
	Rollerball EA, Laparoscopic Bilateral Tubal Ligation	After	Yes, additional Essure procedural time and additional or alternate equipment used to accomplish both procedures
	Rollerball EA	Before	No
	Rollerball EA	Before	No
	Polyp removal (initially interfered with visualization)	After	Yes, additional Essure procedural time and additional or alternate equipment used to accomplish both procedures (had to change to cautery loop)
	Adhesion band over right ostia removed	Before	Yes, additional or alternate equipment used to accomplish both procedures
	Fluffy endometrium on left obscuring view. Tissue removed with grasper.	Before	Yes, additional or alternate equipment used to accomplish both procedures
	Pt with bilateral veiled ostia-grasper used to identify bilaterally	Before	Yes, additional or alternate equipment used to accomplish both procedures
	Polyp obstructing view-removed with grasper-removed piecemeal and sent to pathology	Before	Yes, additional Essure procedural time to grasp and polyp dislodge
	Fibroid/Polyp removal	After	No
	Thermachoice EA	After	No
	Thermachoice EA, Fibroid/Polyp removal	After	No
	LEEP (cervical electrocautery)	After	No
	Hydrothermal EA (HTA), Fibroid/Polyp removal, Laparoscopy myomectomy Burch cysto	After	No
	right salpingo-oophorectomy, micro laparoscopic pain mapping, cystoscopy	micro-lap pain map before, salpino-oophorecotmy After	No
	Hydrothermal EA (HTA)	After	No
	Thermachoice EA, Fibroid/Polyp removal, laparoscopy excision of endometriosis	After	Yes, required different anesthesia method or drugs. Additional or alternate Equipment used to accomplish both procedures

Exhibit C. Concomitant Procedure Data (Cont'd)

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

Exhibit C. Concomitant Procedure Data (Cont'd)

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

Exhibit C. Concomitant Procedure Data (Cont'd)

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

EXHIBIT D: DEVICE ISSUES AND MALFUNCTIONS

Exhibit D. Device Issues and Malfunctions

Patient No. and Physician	Lot No. and AR No.	Date of Occurrence	Device Returned?	Issue or Malfunction Description	Evaluation Results
(b)(4), (b)(6)				Device did not deploy on the right had to use second device. Malfunction may have been secondary to forward pressure on device and angulation of catheter. Tubal spasm was present.	No product returned for evaluation. During conversation and on the returned correspondence, physician noted no other procedural difficulties that would have provided a clear cause for the deployment issue. Retraction was considered normal and the device was easily removed from the tube after the failure to expand. The lot history record shows the device was manufactured and released to the appropriate specifications. No other ARs regarding deployment difficulty have been opened for this lot. Physician reports failure of the device to deploy and no other procedure abnormalities. Possible causes for non-deployment include: deformed or improperly overlapping outer coil, outer coil improperly annealed, outer coil band stuck on the solder/rail, bump stuck in release catheter. Excess tissue on or in the coil may also impair expansion. It was not possible to determine a definite cause for the failure without examining the insert.
				2 attempts at right placement as, when deploying device, it came out of tube on first attempt. Difficulty disconnecting device from delivery system on right with some separation of dacron fiber from coil	No product returned for evaluation. Several root causes were previously identified as causes of detachment difficulty. The primary mode is due to longitudinal strands of fiber wrapping around the delivery wire during the placement procedure. This failure mode was addressed through PMA supplement #P020014/S2 and S3. On (b)(6) a new fibering technique was introduced into the manufacturing process to help elleviate detachment issues between the micro-insert and delivery wire. This Post Approval Study case used an Essure System with the old fibering method and is thus known to be associated with detachment difficulty.
				First device deployed but did not release-came out	No devices returned for evaluation. No further information provided by physician. The lot history record shows the device was manufactured and released to the appropriate specifications. Detachment difficulties may be exacerbated by tubal tortuosity, fiber interference or component deformation. This AR will be added to the CAPA investigating disengagement / detachment difficulties, CAPA 03-035.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4); (b)(6)	Left placement x3 due to non-release of device	No product returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. CRF notes that it was necessary to attempt placement 3 times on the left side due to "non-release" of device. It is not clear whether there were disengagement or detachment issues, but these devices will be included in the investigation of disengagement difficulties covered under CAPA 03-035.
	Difficult release with micro-insert	No product returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. CRF notes "Difficult release with right spring." It is not clear whether there was a disengagement or detachment issues, but this device will be included in the investigation of disengagement difficulties covered under CAPA 03-035.
	Essure device tip damaged with introduction into hysteroscope	No product returned for evaluation. Based on study data, the device was used with a Circon ACMI 5.5 mm OD scope. Introducer testing performed in-house (refer to DR-080) does not show any unusual incidence of introducer or device tip damage with the Circon scope. The lot history record shows the device was manufactured and released to the appropriate specifications. Note on CRF states that there was an issue with the "introducer guide". An introducer can be damaged upon insertion if it is not properly supported by the mandrel. A device tip can be bent if it is not inserted into the introducer correctly, if the introducer is not seated correctly, or if the introducer has been damaged.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	Spontaneous detachment of micro-insert through right tube/ostium	The physician reported that he cannulated the first tube which was slightly lateral. He thumbwheeled back to a stop, but did not see any orange catheter. He suspected that he may have accidentally fed the device forward and began to retract the device from the tube expecting to see the orange release catheter. As he pulled back the micro-insert came off of the delivery wire and disappeared like a "salmon heading up stream". The reported that the button was never depressed, the thumbwheel was not wheeled back a second time, nor was the handle ever rotated to release the device. The patient was a high risk for a laparoscopic procedure due to previous surgeries and weight, so the physician decided to place another device, which was done without incident. Device was returned with a pouch sticker Lot Number (b)(6) Only one device returned. No micro-insert returned. Damage is seen on the catheter shaft in three spots proximal to the marker. The catheter is slightly bent at this area. Delivery wire is slightly curved distal to the rail. Contrary to the physician report, the catheter was returned with the button fully depressed and the catheter is fully retracted. Insert appears to have exited the release catheter straight. The lot history record shows the device was manufactured and released to the appropriate specifications. This may not be a deployment issue, but confusion on the part of the physician's recollection of all the micro-insert placement steps. However, premature deployment may have been caused by retracting across a catheter bend. While there is not significant damage proximal to the marker, there are kink points that may have deformed the release catheter enough to release the insert during retraction.
	Three Essure devices used until successful insertion (tubal spasm caused bent tips)	No product returned. Bent tips are considered by physicians to be a nuisance issue - not a failure of the device to meet manufacturing or performance specifications (no device defect alleged).

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	The first device, placed well, mis-fired and remained attached to the delivery catheter and did not release. Second device bent.	No product was returned for evaluation. Device produced with the "new" fibering method. The lot history record shows the device was manufactured and released to the appropriate specifications. In correspondence, the physician describes a detachment issue, and not an uncoiling/deployment problem. No other factors appeared to be involved in the detachment issue. The micro-insert was pulled out along with the delivery wire, and another device was placed afterwards. Detachment difficulties may be exacerbated by tubal tortuosity, fiber interference or component deformation. This AR will be added to the CAPA investigating disengagement / detachment difficulties, CAPA 03-035.
	Initially placed device into right tube could not be detached from cable and required removal and placement of a second device (successful)	No micro-insert returned. Handle components are fully retracted. Rail shows stretch and displacement near solder area. OD at displacement is 0.023". Outer coil band ID spec = 0.023" +/- 0.0005". Ink at positioning marker shows rubbing. In the fully retracted position, delivery catheter shows wear marks at handle interface. The lot history record shows the device was manufactured and released to the appropriate specifications. Two other ARs have been opened for this lot: one for a bent tip, and one for detachment, with the same physician. Detachment issue reported. It is unclear if the rail displacement occurred before or after detachment attempts, but if the displacement occurred before placement, this may have hampered detachment. The rail damage may also have occurred if the physician attempted to use the hysteroscope tip to brace against the coils and physician reported unsuccessfully using this troubleshooting method. Detachment difficulties may also be caused by tubal tortuosity and fiber interference.
	Again difficulty with release of the cable from the micro-insert after deployment. However, with several minutes of revolutions, cable did separate and bilateral placement achieved.	Device 1 returned without micro-insert. Remainder of catheters and wire in good condtion. Blocker coil is close (< 1 blocker coil width) to release catheter hole. Handle components are fully retracted. Device 2 returned without micro-insert. Release catheter has kink halfway between hole and delivery catheter tip. Remainder of catheters and wire in good condtion. Handle components are fully retracted. The lot history record shows the device was manufactured and released to the appropriate specifications. Detachment issues reported. Physician achieved detachment after additional rotations with the handles. The core wire bend can indicate a difficult cannulation, which may have contributed to the detachment difficulty. No clear causes found for the detachment issues. Detachment difficulties may be exacerbated by tubal tortuosity, fiber interference or component deformation.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	Two devices failed. One failed to release delivery wire and second tip became unraveled after insertion into tubal ostium before deployment: both from same Lot.	Device 1 returned without micro-insert. Remainder of catheters and wire in good condition. Blocker coil is close (< 1 blocker coil width) to release catheter hole. Handle components are fully retracted. Device 2 returned without micro-insert. Release catheter has kink halfway between hole and delivery catheter tip. Remainder of catheters and wire in good condition. Handle components are fully retracted. The lot history record shows the device was manufactured and released to the appropriate specifications. Detachment issues reported. Physician achieved detachment after additional rotations with the handles. The core wire bend can indicate a difficult cannulation, which may have contributed to the detachment difficulty. No clear causes found for the detachment issues. Detachment difficulties may be exacerbated by tubal tortuosity, fiber interference or component deformation.
	The first Essure tip was bent as it was placed through the hysteroscope and was discarded	No product returned for evaluation. Bent tip during introduction reported.
	One implant not used because tip was bent in insertion attempt on the left tube. Left tube had a lateral orientation	No product returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. Physician reported device tip was bent during attempted cannulation of a lateral tube.
	Right ~ 2 devices would not release	Both devices returned were Gamma catheters. One device had delivery catheter damage, preventing retraction, other device did not show any damage. Device 1: No micro-insert returned. Rail coil shows bending. Last turn and gap width are in spec by measurement with calipers. Delivery catheter shaft twisted 1 and 2 cm proximal to positioning marker. Twisting appears to be in a clockwise direction, but it is not clear when the twisting occurred. Rail coil does not show evidence of having been opened up by clockwise turning. Twisting not noticed on release catheter and retraction is not restricted. Handle components are in fully retraction position. Device 2: No micro-insert returned. Rail coil appears undamaged. Last turn and gap width are in spec by measurement with calipers. Remainder of catheter appears in good condition. Handle components are in fully retraction position. Bending of the device, as evidenced on Device 1, may have contributed to disengagement difficulties. Catheter shaft twisting in the clockwise direction was noted, but corresponding rail coil deformation was not noted. For both devices, a clear cause for the disengagement problems was not evident. This AR will be added to the CAPA 03-035 investigating disengagement-detachment issues.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	Left ~ Failure to deploy/release	Four Coil catheters (ESS205) were returned. One is not at all retracted, and deployed normally on the bench. Other 3 did not have micro-inserts and appear normal. Device 1: Catheter returned with micro-insert, unretracted and in good condition. Catheter was retracted on the bench, and the micro-insert deployed and detached normally. The lot history record shows the device was manufactured and released to the appropriate specifications. No deployment issues found with this catheter. Devices 2, 3 and 4 No micro-inserts returned. All catheters returned fully retracted and in good condition. All blocker coils met OD specifications and showed no evidence of interference with the outer coil band. All inserts appear to have made a straight exit. The lot history record shows the device was manufactured and released to the appropriate specifications. Deployment difficulties could not be confirmed for these devices. Possible causes for non-deployment include: deformed or improperly overlapping outer coil, improper outer coil annealing, outer coil band interference with the solder/rail, bump unable to move away from release catheter. Excess tissue on or in the coil may also impair expansion. No clear causes could be found for deployment difficulties, but complaints of this nature will continue to be monitored.
	Left tube Essure did not release and was withdrawn New implant inserted without difficulty.	No device returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. Detachment difficulty reported on CRF. Insert was removed and replaced without difficulty. No clear causes for the difficulty were found in the report forms. Detachment difficulties may be exacerbated by tubal tortuosity, fiber interference or component deformation.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	Guide wire would not detach. Inner sleeve detached and had to be manually removed. Trailing coils distorted secondary to difficulty removing wire	No device returned for evaluation. Device used "new" fibering method. The lot history record shows the device was manufactured and released to the appropriate specifications. In conversation, the physician described a lengthy cannulation of a tube "at an angle". He had difficulties with detachment and continued to turn the handle until the insert did detach. Detachment issues were likely exacerbated by the difficult cannulation. The delivery catheter may have suffered damage before detachment due to the access issue, and was worsened by retraction and rotations. The delivery catheter ("inner sleeve" in the description) broke in the distal area and the separated piece was retrieved. The micro-insert remains in the patient.
	Manufacturing difficulties in Essure catheter, Thumb wheel did not go back easily on right side catheter, and post detachment difficulties	No product returned for evaluation. LHR shows that the device is a coil catheter with a screw handle. The lot history record shows the device was manufactured and released to the appropriate specifications. Physician reports a rollback difficulty, followed by a detachment difficulty with the same device. She has reported that in these circumstances, she would ask for assistance in forcing the thumbwheel back, and then continue with the procedure. There were no particular circumstances described that would have contributed to the detachment difficulties.
	Difficulty moving thumb wheel back, which may have had detachment difficulty of coil on right side	No product returned for investigation. This AR will be added to the CAPA investigating thumbwheel rollback difficulties, CAPA 04-008. Detachment / disengagement issues will be addressed by the New Release Mechanism project. See DP-0027 for Development Plan.
	Detachment difficulty with right Essure catheter, 15 coils exposed in right tube	No product returned for investigation. Unable to verify detachment issue.
	Detachment difficulty	No product returned for investigation. Unable to verify detachment issue.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(4), (b)(6)	Thumbwheel stuck on one catheter, some detachment difficulty	No product returned for evaluation. LHR shows that the device is a coil catheter with a screw handle. The lot history record shows the device was manufactured and released to the appropriate specifications. Physician reports a rollback difficulty and a detachment difficulty. It is not clear if they occurred with the same device. She has reported that in these circumstances, she would ask for assistance in forcing the thumbwheel back, and then continue with the procedure. There were no particular circumstances described that would have contributed to the detachment difficulties.
	Left - 12238561 Original intro catheter failed to retract. Device from same lot successfully placed.	No product returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. Physician reports "introducer" catheter (delivery catheter) failed to retract. In correspondence with (b)(6) he indicates that there was no difficulty with cannulation and no kinking - the thumbwheel moved very slightly, and then stuck. This may indicate that the thumbwheel was able to rock back and forth slightly, as it is able to do before engaging the detent. The "stuck" feeling may be the inability to move past the initial click of the detent. This device will be added to the CAPA investigation covering the thumbwheel initiation difficulty.
	Catheter was placed in the right tube and would not release. Pulled right out, needed new catheter which was placed without difficulty	No device returned for evaluation, and no further information was available from the physician. Catheter produced with "new" fibering method. The lot history record shows the device was manufactured and released to the appropriate specifications. CRF reports that "Catheter was placed in the right tube and would not release. Pulled right out, needed new catheter which was placed without difficulty." We will interpret this to mean that the micro-insert would not detach from the wire. Detachment difficulties may be caused and exacerbated by fiber interference, tubal tortuosity or component deformation or interference.

Exhibit D. Device Issues and Malfunctions (Cont'd)

(b)(6)	Device seemed to release too easily today. I felt like counter clockwise rotation was not required to release the catheters	No device returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. PAS Physician noted in CRFs that he felt counterclockwise rotations were not required to release the catheter. There is currently no specification for a minimum number of turns required to disengage the insert. The lot release testing for the associated lot of catheters (b)(6) shows that out of a test sample of 2, 1 device disengaged at 1 turn and 1 device disengaged at 1.5 turns. These are both acceptable.
	Tip bent, needed to open and use another catheter	No device returned for evaluation. The lot history record shows the device was manufactured and released to the appropriate specifications. Bent tip reported on PAS CRF. It is unspecified how or when the bend occurred. Tip bending is well-understood and can occur during a procedure for several reasons, including difficulties in removal from packaging, difficulties or interference during introduction and cannulation, and scope interference. Bilateral placement was ultimately achieved.

EXHIBIT E: DETAILED ANALYSIS OF PLACEMENT FAILURES WITH CONCLUSION

Exhibit E. Detailed analysis of placement failures with conclusion

(b)(4), (b)(6)	
Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a (b)(6) BMI of 23, grava 3, para 2, with 2 vaginal births and 1 induced abortion. She had no prior abdominal surgery or other OB/GYN conditions that required treatment. No prior PID, salpingitis or STD. The patient was post-partum, having delivered on 7/17/03. In violation of the Post Approval Study Protocol, the Essure placement procedure was performed 5 weeks (36 days) later on 8/22/03. According to the Essure physician literature, the Essure System should not be used in any patient having delivery or termination of pregnancy less than 6 weeks before Essure micro-insert placement. The patient was provided injectable progesterone (Depo-Provera) only a few days prior to the Essure procedure. At the time of the procedure, she was placed under local anesthesia with IV sedation (Toradol) in a hospital-based procedure room. An NSAID (Toradol) was provided prior to the procedure. A 5.0mm Storz hysteroscope was used with saline distension media using a pump. The hysteroscopic procedure time was recorded as 50 minutes in duration with no concomitant procedures or adverse events and a total fluid deficit of 690cc. No Essure devices were placed due to poor distension with endometrium preventing proper visualization of both tubal ostia.
Conclusion	The most likely cause associated with this occurrence of bilateral placement failure was pathologic, with inability to visualize tubal ostia due to thick endometrium in a contra-indicated post-partum patient that prevented ostial visualization. In addition to the poor timing, novice hysteroscopic technique was evident in this first case (post preceptored training) by distension problems, relatively high fluid deficit and long procedure time.

(b)(4), (b)(6)	
Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a (b)(6), BMI of 30.1, grava 3, para 2, with 3 vaginal births. She had prior abdominal cholecystectomy in 1981 and cervical cryosurgery for dysplasia in 1996. No prior PID, salpingitis or STD. Her LMP was 1/18/03 and she was on day 40 of her menstrual cycle at the time of Essure placement on 2/27/03. The patient was on oral contraceptives for greater than one year prior to the Essure procedure. There was no other hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under local anesthesia with IV sedation in a hospital-based procedure room. An NSAID was not taken prior to the procedure, contrary to the strong recommendation in the Essure physician literature. A 5.5mm ACMI hysteroscope was used with saline distension media using a pressure bag. The hysteroscopic procedure time was recorded as 44 minutes in duration with no concomitant procedures or adverse events and a total fluid deficit of 500cc. No Essure devices were placed due to the inability to visualize the left tubal ostium (primary cause) with tubal obstruction/spasm on the

right.

Conclusion The most likely cause associated with this occurrence of bilateral placement failure was pathologic, with thick endometrium on the 40th day of the patients' menstrual cycle preventing visualization of the left tubal ostium. In addition to the poor timing, the patient was not prescribed an NSAID one to two hours before the micro-insert placement procedure, which could have prevented tubal spasm. Prior clinical trial data demonstrate that the use of NSAIDs significantly increase the likelihood of placement success. Lastly, novice hysteroscopic technique was evident in this first case (post preceptored training) by a relatively high fluid deficit and long procedure time.

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

Issue Bilateral micro-insert placement failure

Operative Report Patient is a (b)(6), BMI of 35, grava 1, para 0, with 1 spontaneous abortion. She had prior diagnostic laparoscopy for infertility in 10/96; hysteroscopy/D&C for menorrhagia in 8/99; hysteroscopy for tubal insuflation and laparoscopic lysis of adhesions on 8/00. No prior PID, salpingitis or STD. Her LMP was 4/9/03 and she was on day 7 of her menstrual cycle at the time of Essure placement on 4/16/03.

The patient was not using any contraceptive method prior to the Essure procedure. There was no hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under local anesthesia with IV sedation in a hospital-based procedure room. An NSAID was not taken prior to the procedure, contrary to the strong recommendation in the Essure physician literature. A 5.5mm ACMI hysteroscope was used with saline distension media using a pressure bag. The hysteroscopic procedure time was recorded as 27 minutes in duration with no concomitant procedures or adverse events and a total fluid deficit of 100cc. No Essure devices were placed due to the tubal obstruction/spasm of the left fallopian tube and the ostium was not visible on the right. Subsequently, the fallopian tubes were seen at laparoscopy to be "horizontal".

Conclusion The most likely cause associated with this occurrence of bilateral placement failure is anatomic, with fallopian tubes lateral to the uterus that contributed to visualization and cannulation difficulty. Additionally, the patient was not prescribed an NSAID one to two hours before the micro-insert placement procedure, which could have prevented tubal spasm. Prior clinical trial data demonstrate that the use of NSAIDs significantly increase the likelihood of placement success. A confounding factor for lack of ostial visualization according to Dr. Rafael Valle, investigator in the Pivotal Clinical Trial, is insufficient distension (pressure to open the tubes).

(b)(6)	
Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a (b)(6) BMI of 23.1, grava 4, para 3, with 3 vaginal births and 1 spontaneous abortion. She had no prior abdominal surgery or other OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 12/22/04 and she was on day 7 of her menstrual cycle at the time of Essure placement on 12/29/04. The patient was using oral contraceptives for 3-6 months prior to the Essure procedure. There was no other hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under IV sedation in a hospital-based procedure room. An NSAID (Toradol) was provided prior to the procedure. A 5.0mm Storz hysteroscope was used with saline distension media using a pump. The hysteroscopic procedure time was recorded as 31 minutes in duration with no concomitant procedures or adverse events and a total fluid deficit of 90cc. No Essure devices were placed due to tubal ostia being located laterally and preventing micro-insert placement.
Conclusion	The most likely cause associated with this occurrence of bilateral placement failure is anatomic, with fallopian tubes lateral to the uterus that contributed to visualization and cannulation difficulty.

(b)(4), (b)(6)	
Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a (b)(6) BMI of 34, grava 1, para 2, with 1 caesarian. She had no prior abdominal surgery or other OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 7/23/03 and she was on day 34 of her menstrual cycle at the time of Essure placement on 8/26/03. The patient was relying on condoms for contraception prior to the Essure procedure. There was no hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under IV sedation with local anesthesia in an outpatient surgery center. An NSAID (Vioxx) was taken prior to the procedure. A 5.0mm Olympus hysteroscope was used with saline distension media using gravity feed. The hysteroscopic procedure time was recorded as 29 minutes in duration with no adverse events and a total fluid deficit of 1100cc. The tubal ostia were located laterally, preventing micro-insert placement in the left tube. The right tube was not attempted. Laparoscopic tubal ligation with Falope rings was performed after the attempted Essure placement procedure. The left tube was observed to be scarred at the isthmus, preventing device placement.
Conclusion	The most likely cause associated with this occurrence of bilateral placement failure is anatomic, with fallopian tubes lateral to the uterus that contributed to visualization and cannulation difficulty. Uterine pathology was a likely contributor to visualization and cannulation difficulty due to placement on day 34 of the patient's menstrual cycle. In addition to the poor timing, poor hysteroscopic technique was evidenced by large fluid deficit and relatively long procedure time.

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

Issue Bilateral micro-insert placement failure

Operative Report Patient is a (b)(6) BMI of 20.6, grava 4, para 0, with 4 induced abortions. She had no prior abdominal surgery or other OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 3/7/03 and she was on day 83 of her menstrual cycle at the time of Essure placement on 5/29/03.

The patient was relying on injectable progesterone (Depo-Provera) for contraception for less than 3 months that was also prescribed for manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under IV sedation in a hospital based procedure room. An NSAID was not taken prior to the procedure, contrary to the strong recommendation in the Essure physician literature. A 5.0mm Storz hysteroscope was used with saline distension media using a pump. The hysteroscopic procedure time was recorded as 35 minutes in duration with no adverse events and a total fluid deficit of 340cc. No Essure devices were placed due to tubal obstruction/spasm of the right fallopian tube.

Conclusion The most likely cause associated with this occurrence of bilateral placement failure is not known. However, the patient was not prescribed an NSAID one to two hours before the micro-insert placement procedure, which could have prevented tubal spasm. Prior clinical trial data demonstrate that the use of NSAIDs significantly increase the likelihood of placement success. A confounding factor for placement failure in this case may include technique issues such as insufficient distension (pressure to open the tubes) or unsatisfactory endometrial pathology because the placement procedure was performed on day 83 of the patient's menstrual cycle. In addition to the poor timing, the patient was injected with Depo-Provera less than 3 months prior to the Essure procedure. Depo takes a long time, 6 months or more, to thin the endometrium and can compound intrauterine problems in the early months.

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

Issue Bilateral micro-insert placement failure

Operative Report Patient is a (b)(6) n, BMI of 30, grava 3, para 3, with 3 vaginal births. She had no prior abdominal surgery or other OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 12/3/03 and she was on day 9 of her menstrual cycle at the time of Essure placement on 12/12/03.

The patient was relying on oral contraceptives for contraception for more than a year prior to the scheduled Essure procedure. At the time of the procedure, she was placed under general anesthesia in an outpatient surgery center. An NSAID (Toradol) was provided prior to the procedure. A 7.0mm Circon hysteroscope was used with saline distension media using a pump. The hysteroscopic procedure time was recorded as 26 minutes in duration with no adverse events and a total fluid deficit of 250cc. No Essure devices were placed due to failure to deploy/release the micro-insert in the left tube. Laparoscopic bilateral tubal ligation was performed immediately following the failed Essure placement.

Conceptus Investigation Results	Four Coil catheters (ESS205) were returned. One is not at all retracted, and it was subsequently deployed normally on the bench. The other 3 did not have micro-inserts and otherwise appear normal. Device 1: Catheter returned with micro-insert, unretracted and in good condition. Catheter was retracted on the bench, and the micro-insert deployed and detached normally. The lot history record shows the device was manufactured and released to the appropriate specifications. No deployment issues were found with this catheter. Devices 2, 3 and 4 No micro-inserts returned. All catheters were returned fully retracted and in good condition. All blocker coils met OD specifications and showed no evidence of interference with the outer coil band. All inserts appear to have made a straight exit. The lot history record shows the device was manufactured and released to the appropriate specifications. Deployment difficulties could not be confirmed for these devices. Possible causes for non-deployment include: deformed or improperly overlapping outer coil, improper outer coil annealing, outer coil band interference with the solder/rail, bump unable to move away from release catheter. Excess tissue on or in the coil may also impair expansion. No clear causes could be found for deployment difficulties, but complaints of this nature will continue to be monitored.
Conclusion	The reported cause associated with this occurrence of bilateral placement failure is failure of one micro-insert to deploy/release. However, the root cause of the deployment/release difficulty could not be identified or even confirmed from the returned product. According to Dr. Rafael Valle, investigator in the Pivotal Clinical Trial, an unusually large diameter hysteroscope was used in this case. The cervix must be dilated more to accommodate large diameter scopes and they are known to increase the difficulty of tubal cannulation.

(b)(4), (b)(6)	
Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a (b)(6), BMI of 39, grava 1, para 1 with 1 cesarean on 5/81. She had no other previous abdominal surgery or OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 12/19/03 and she was on day 11 of her menstrual cycle at the time of Essure placement on 12/30/03. The patient was not using any contraceptive method for over one year prior to the Essure procedure. There was no hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under general anesthesia with local anesthesia in an outpatient surgery center. An NSAID (Toradol) was provided prior to the procedure. A 6.5mm Storz hysteroscope was used with saline distension media using a pressure bag (gravity feed is recommended in the Essure physician literature). The hysteroscopic procedure time was recorded as 21 minutes in duration with no concomitant procedures and no adverse events. The

	patient had unusual uterine anatomy with very large diameter tubal ostia on both sides. The physician attempted placement on the left (larger ostia) first. The uncoiled, released diameter of the Essure micro-insert was smaller than the diameter of the ostia. Physician did not attempt the right side and converted to laparoscopic tubal ligation at the patient's request. The patient had small fibroids, but otherwise normal anatomic appearance.
Conclusion	The most likely cause associated with this occurrence of bilateral placement failure is anatomic, with large diameter fallopian tubes that prevented acute micro-insert anchoring.

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

Issue	Bilateral micro-insert placement failure
Operative Report	Patient is a nulliparous (b)(6) BMI of 16.5, grava 0, para 0. She had no previous abdominal surgery or OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 10/2/03 and she was on day 12 of her menstrual cycle at the time of Essure placement on 10/14/03. The patient was relying on oral contraceptives for over one year prior to the Essure procedure. There was no other hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was given IV sedation in an outpatient surgery center. An NSAID was not taken prior to the procedure, contrary to the strong recommendation in the Essure physician literature. A 3.7mm Circon hysteroscope was used with saline distension media using a pump (gravity feed is recommended in the Essure physician literature). The hysteroscopic procedure time was recorded as 26 minutes in duration with no concomitant procedures. The physician reported that the fallopian tubes were too lateral, preventing micro-insert placement and the fluid deficit was too great to continue. Laparoscopy failed to show the location of the excess fluid (1800cc), but the patient did well. No Essure devices were placed and the patient underwent bilateral tubal occlusion with banding. The patient was monitored in recovery for about 4 hours, her electrolytes were checked and she did not show any untoward effects and was able to go home that evening. The physician worked along with the anesthesiologist to assess her fluids, and the anesthesiologist agreed that she was stable. She was given a dose of Lasix 10mg IV, and she put out a good amount of urine as a result. Her lung exam, vital signs, and pulse oximetry readings were all normal.
Conclusion	The most likely cause associated with this occurrence of bilateral placement failure is anatomic, with fallopian tubes lateral to the uterus that contributed to visualization and cannulation difficulty. Additionally, novice hysteroscopic technique was evident in this first case (post preceptored training) by very high fluid deficit and relatively long procedure time. The 3.7mm Circon hysteroscope, according to Dr. Rafael Valle, is too small to adequately circulate distension fluid in the working channel annulus around the Essure delivery catheter shaft.

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

Issue Bilateral micro-insert placement failure

Operative Report Patient is a (b)(6) BMI of 26.8, grava 2, para 2 with 2 vaginal births. She had no other previous abdominal surgery or OB/GYN conditions requiring treatment. Prior PID, salpingitis or STD is unknown. Her LMP was 9/18/03 and she was on day 21 of her menstrual cycle at the time of Essure placement on 10/9/03.

The patient relied on a contraceptive patch for less than 3 months prior to the Essure procedure. There was no other hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was placed under general anesthesia in a hospital based procedure room. An NSAID was not taken prior to the procedure, contrary to the strong recommendation in the Essure physician literature. A 5.5mm Olympus hysteroscope was used with saline distension media using a gravity feed. The hysteroscopic procedure time was recorded as 12 minutes in duration with no concomitant procedures and no adverse events. No Essure devices were placed due to tubal obstruction/spasm of both fallopian tubes.

Conclusion The most likely cause associated with this occurrence of bilateral placement failure is reported to be tubal obstruction/spasm of both tubes, but the etiology is not known. However, the patient was not prescribed an NSAID one to two hours before the micro-insert placement procedure, which could have prevented tubal spasm. Prior clinical trial data demonstrate that the use of NSAIDs significantly increase the likelihood of placement success. Additionally, the Essure procedure was performed late in the patient's menstrual cycle, and peak endometrial thickness is known to affect visualization and the timing carries an increased risk of luteal phase pregnancy.

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

Issue Bilateral micro-insert placement failure

Operative Report Patient is a (b)(6) BMI of 29.2, grava 3, para 2 with 2 vaginal births and 1 induced abortion. She had no other previous abdominal surgery or OB/GYN conditions requiring treatment. No prior PID, salpingitis or STD. Her LMP was 10/6/04 and she was on day 5 of her menstrual cycle at the time of Essure placement on 10/11/04.

The patient relied on oral contraceptives for more than one year prior to the Essure procedure. There was no other hormonal manipulation of her endometrium prior to the scheduled Essure procedure. At the time of the procedure, she was given local anesthesia with IV sedation in a hospital based procedure room. An NSAID (Toradol) was provided prior to the procedure. A 5.0mm Olympus hysteroscope was used with saline distension media using a pressure bag. The hysteroscopic procedure time was recorded as 12 minutes in duration with no concomitant procedures and no adverse events. No Essure devices were placed due to tubal obstruction/spasm of both fallopian tubes.

Conclusion	The most likely cause associated with this occurrence of bilateral placement failure was reported to be tubal obstruction/spasm of both tubes, but the etiology is not known (the physician did not elect to perform a post-procedure HSG to assess the fallopian tubes). Confounding factors for placement failure in this case may include technique issues such as insufficient distension (pressure to open the tubes) or pathological issues such as veiled ostia.

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

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

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

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

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

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

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

EXHIBIT F: PRIOR ABDOMINAL SURGERY

Exhibit F. Prior Abdominal Surgery

Patient No.	Prior abdominal/pelvic surgery
(b)(4), (b)(6)	

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

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

EXHIBIT G: CLINICAL STUDY PROTOCOL AND CASE REPORT FORMS

Conceptus®

Essure™ System

US Post-Approval Study for Newly Trained Physicians

Conceptus Protocol:

Essure PAS Placement

Sponsor:

Conceptus Incorporated

1021 Howard Avenue

San Carlos, CA 94070

Telephone 650-628-4700

Fax 650-802-2890

REVISION HISTORY

Version Number	Description of Change	Effective Date
Version	(b)(4)	October 17, 2002
Version		September 30, 2003

Table of Contents

Appendices

1. Title

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

2. Study Purpose

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

3. Study Design

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

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

Physician enrollment in this study will be limited to no more than (b)(4) (b)(4) and no more than (b)(4). In

addition, no more than (b)(4) of the physicians will represent either (b)(4).

The first 45 physicians in (b)(4) in the United States who complete the (b)(4) will be asked to participate in this study. Such physicians will be enrolled in the study only if: 1) they agree to participate, and 2) they do not have previous experience in Essure micro-insert placement. In addition, they will not contribute cases to this study until after they have completed the preceptoring portion of the training program.

The enrolled physicians will then collect demographic and micro-insert placement data on the first cases performed after preceptoring is complete, until placement data are available on a total of (b)(4) women in whom an Essure System was placed through the operating channel of the hysteroscope. Since data on "non-attempts" will also be collected, it is anticipated that more than 800 women will be enrolled in order to obtain data on 800 women with an actual placement attempt.

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

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

4. Primary Endpoints

The primary endpoints are as follows:

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

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

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

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

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

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

5. Designated Person

(b)(4)

6. Inclusion and Exclusion Criteria

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

Additional inclusion criteria:

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

7. Data collection

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

(b)(4)

8. Instructions for Use

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

9. Records and Reports

Records

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

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

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

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

Content and timing of reports

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

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

10. Statistical Analysis and Reporting of Results

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

11. Financial Issues

(b)(4)

(b)(4)

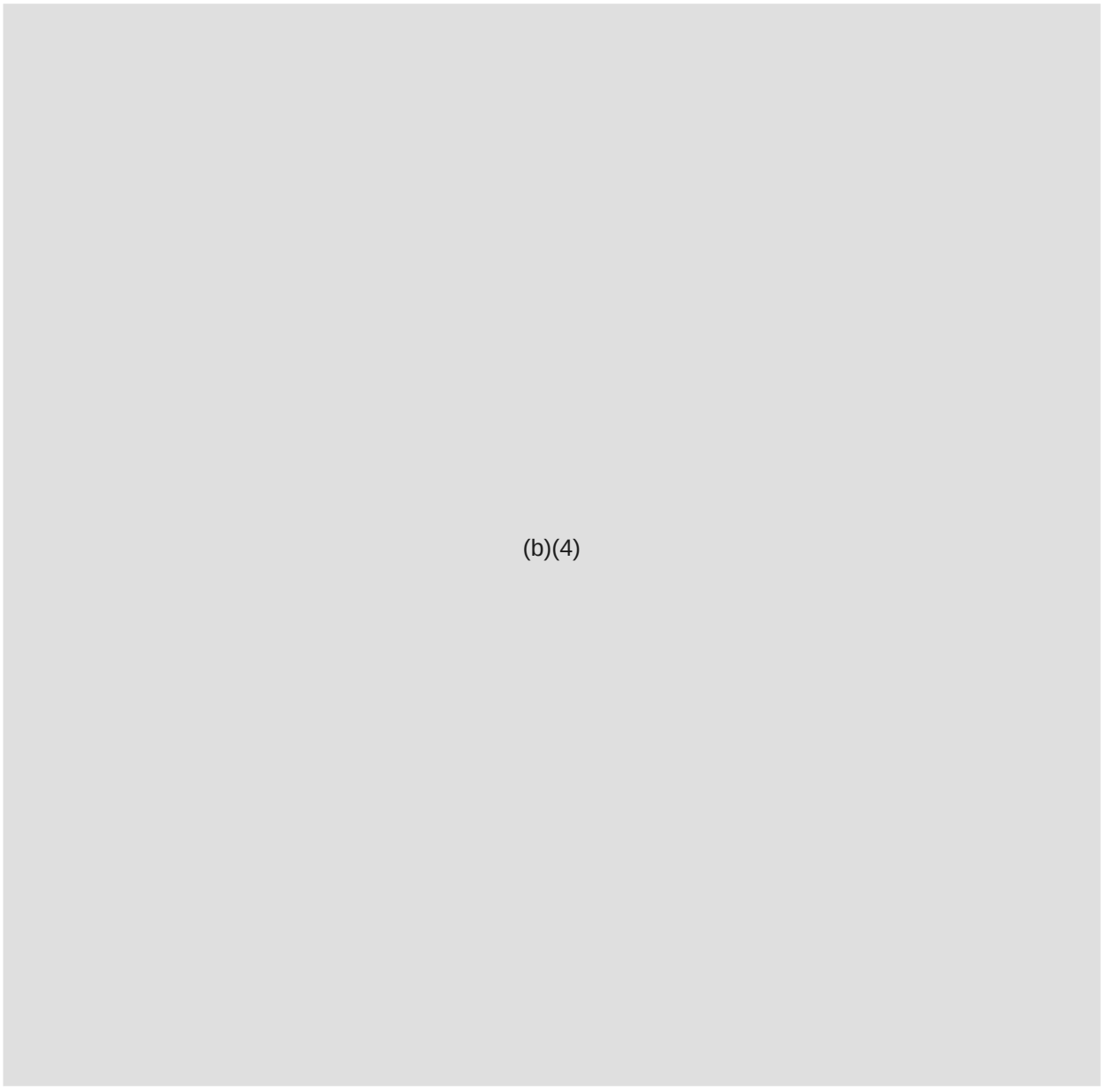
12. Study period

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

Appendix A

Statistical Analysis Plan

(b)(4)



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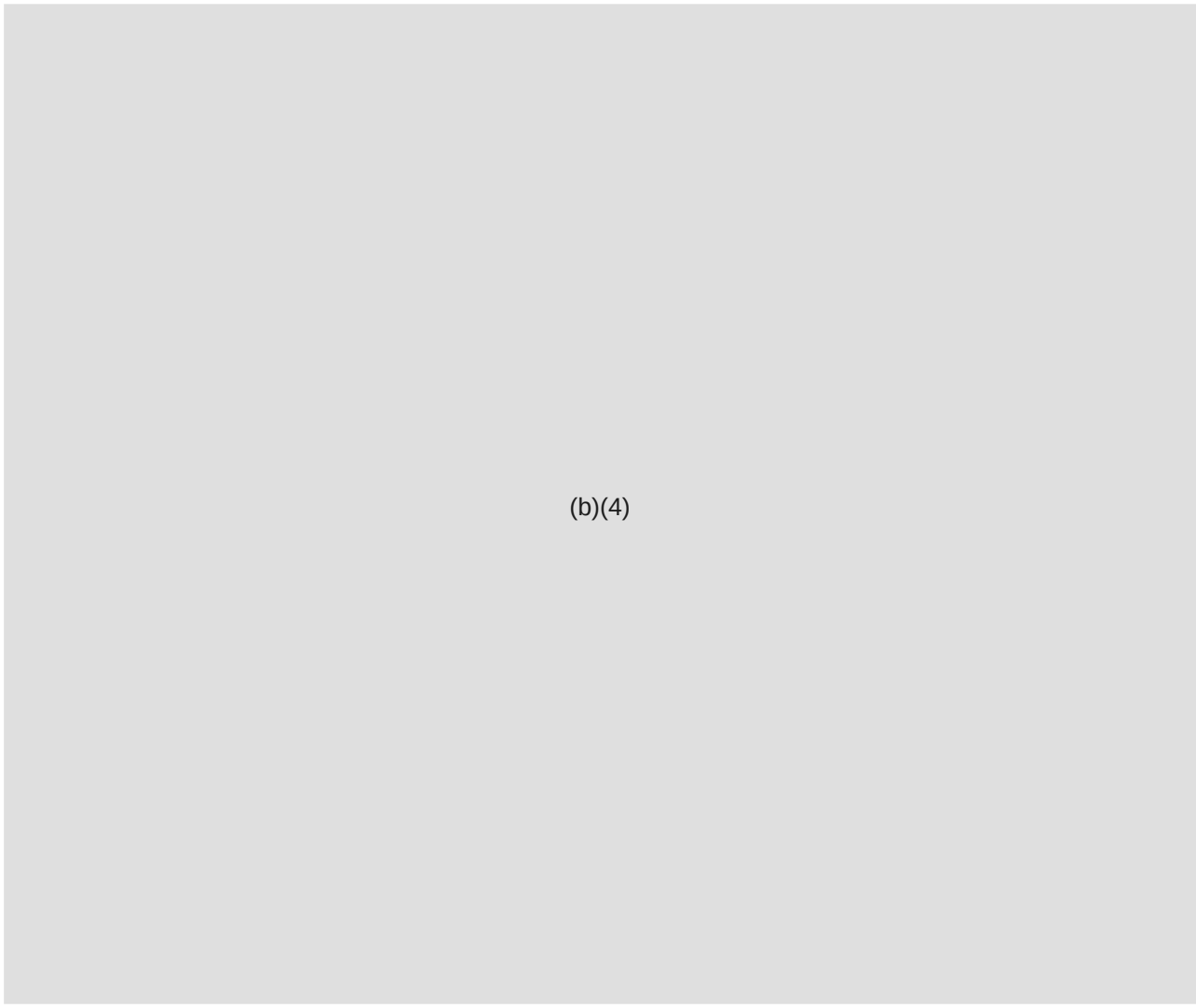
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Appendix B

Case Report Forms

Pages 111 through 121 redacted for the following reasons:
- -
(b)(4)-Trade Secret
Case Report Form (CRF)

Conceptus®

Essure™ System

US Post-Approval Study for Newly Trained Physicians

Conceptus Protocol:

Essure PAS Placement

Sponsor:

Conceptus Incorporated

1021 Howard Avenue

San Carlos, CA 94070

Telephone 650-628-4700

Fax 650-802-2890

REVISION HISTORY

Version Number	Description of Change	Effective Date
(b)(4)	(b)(4)	October 17, 2002
		September 30, 2003

Table of Contents

Appendices

1. Title

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

2. Study Purpose

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

3. Study Design

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

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

Physician enrollment in this study will be limited to no more than (b)(4) (b)(4) In

addition, (b)(4) of the physicians will represent either (b)(4).

The first 45 physicians in in the United States who complete the (b)(4) of the training program will be asked to participate in this study. Such physicians will be enrolled in the study only if: 1) they agree to participate, and 2) they do not have previous experience in Essure micro-insert placement. In addition, they will not contribute cases to this study until after they have completed the preceptoring portion of the training program.

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

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

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

4. Primary Endpoints

The primary endpoints are as follows:

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

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

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

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

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

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

5. Designated Person

(b)(4)

6. Inclusion and Exclusion Criteria

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

Additional inclusion criteria:

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

7. Data collection

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

(b)(4)

8. Instructions for Use

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

9. Records and Reports

Records

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

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

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

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

Content and timing of reports

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

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

10. Statistical Analysis and Reporting of Results

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

11. Financial Issues

(b)(4)

(b)(4)

12. Study period

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

Appendix A

Statistical Analysis Plan

(b)(4)

(b)(4)

(b)(4)

Appendix B

Case Report Forms

Pages 136 through 146 redacted for the following reasons:
- -
(b)(4)-Trade Secret Information
Case Report Forms

Exhibit 2

Placement Rate Summary: Post Approval Study for Newly Trained Physicians

Conceptus®

PLACEMENT RATE SUMMARY: POST APPROVAL STUDY

for Newly Trained Physicians

(b)(6)

Essure PAS – Placement Rates
September 2, 2004
Update February 5, 2005
Update March 14, 2005

Methods

Recruitment

Study participants were women seeking permanent contraception.

Inclusion and Exclusion Criteria

All inclusion and exclusion criteria from the Instructions for Use approved under the Essure PMA (P020014) were used.

Additional inclusion criteria:

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

Treatment

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

Follow-up

No patient follow-up was conducted as part of this study, with the exception of data from follow-up HSGs performed to evaluate the reasons for placement failure in women who desire a second attempt at device placement. Data from the second attempt was not recorded according to the study protocol.

Definitions

Outcomes as they relate to the procedure are defined below. Outcomes are briefly reviewed in the following paragraphs:

- **Rate of non-attempts**: the number of women in whom no device was placed through the hysteroscope.
- **Bilateral placement rate**: the proportion of women in whom bilateral placement is achieved on placing the device through the hysteroscope.
- **Bilateral placement without known confounders**: the proportion of women in whom bilateral placement is achieved, excluding women in whom bilateral placement is subsequently found to be impossible, primarily due to the lack of two anatomic fallopian tubes (e.g., unicornuate uterus).

Study Objectives

The goals of the post-approval study were to:

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

b. identify factors predictive of failure to achieve bilateral placement of the Essure system at first attempt.

In this summary, we also compare the bilateral placement rate with that observed in the pre-approval study.

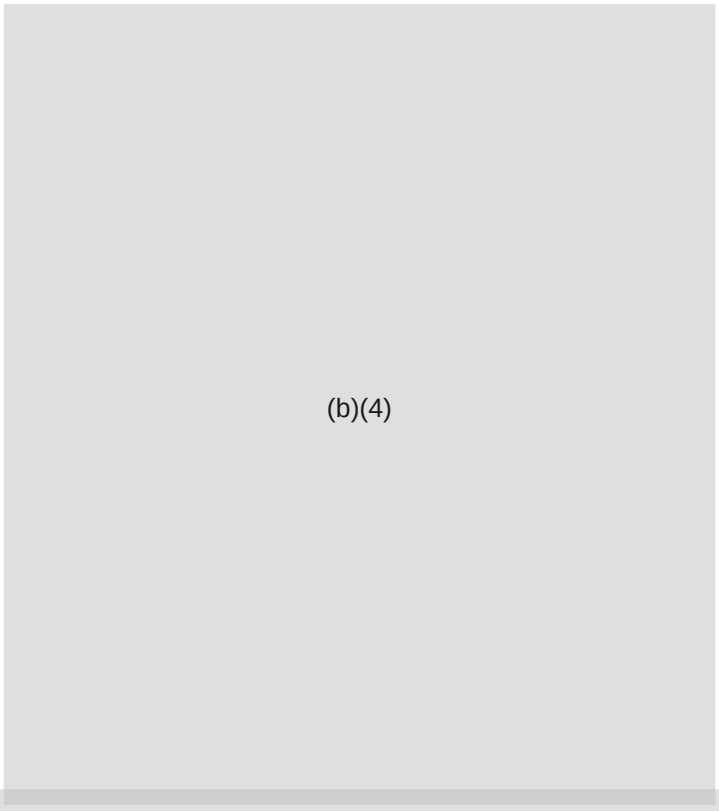
Statistical Summaries

(b)(4)

Results

Physician and Patient Participants

(b)(4)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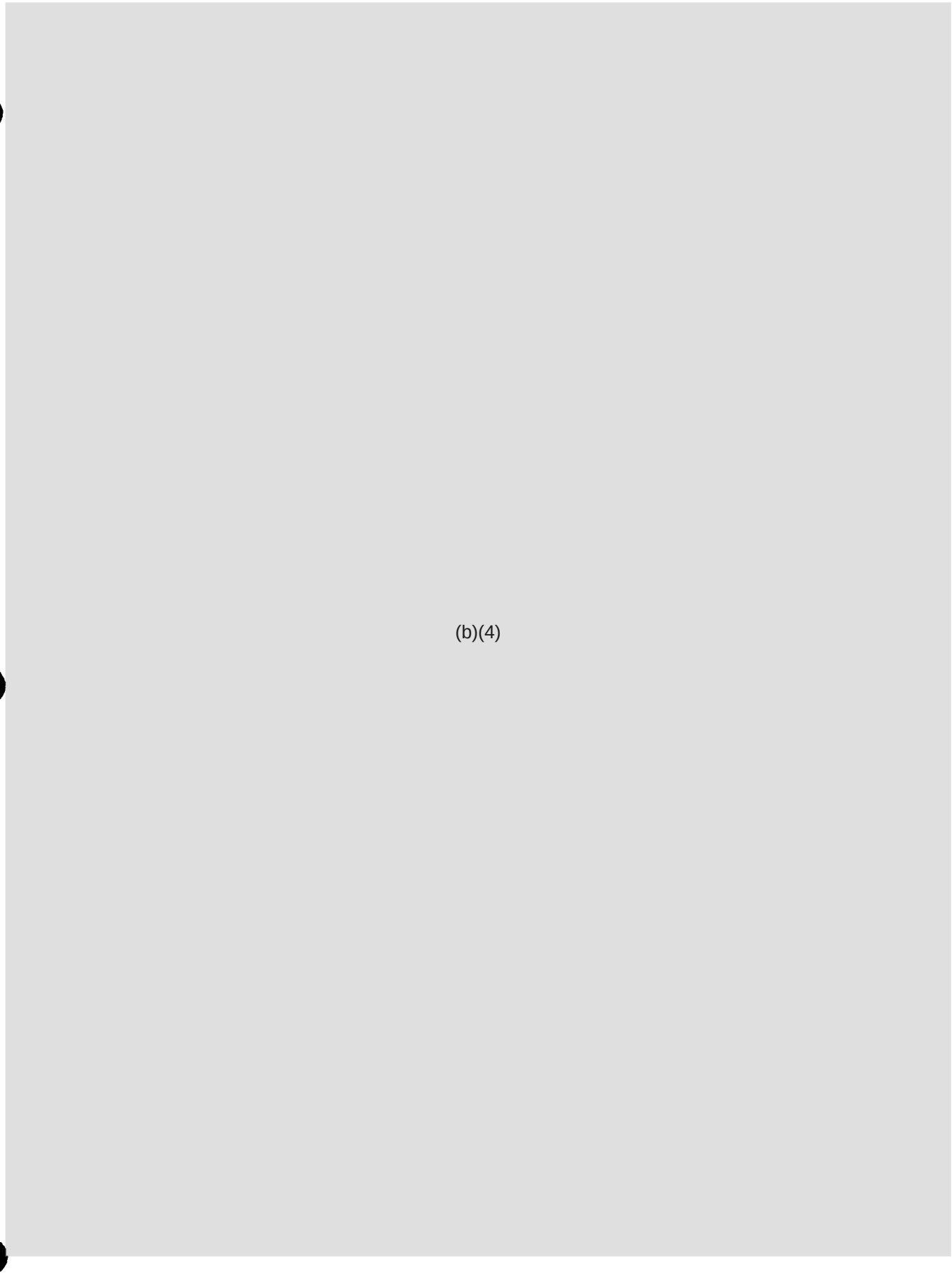
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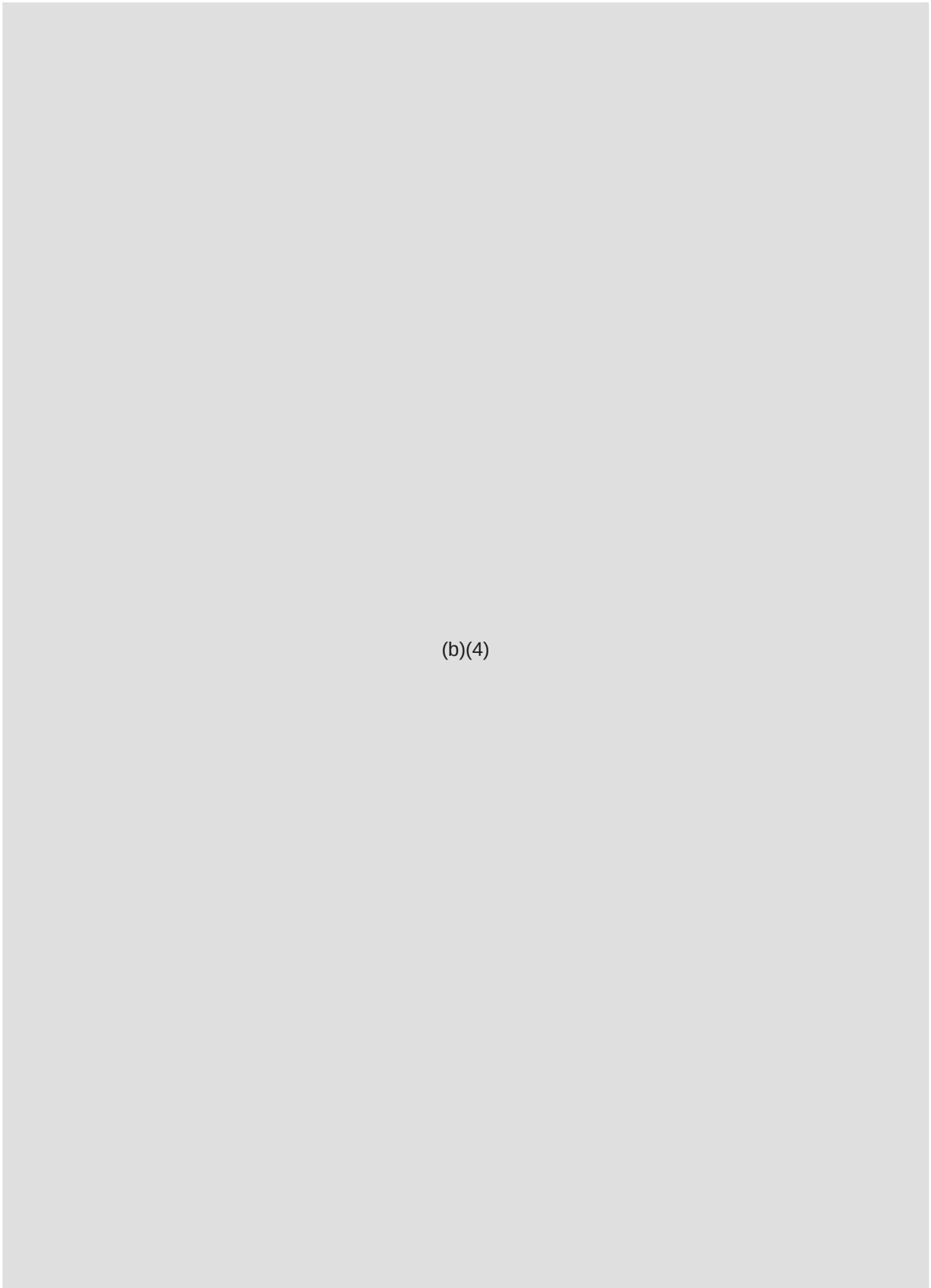
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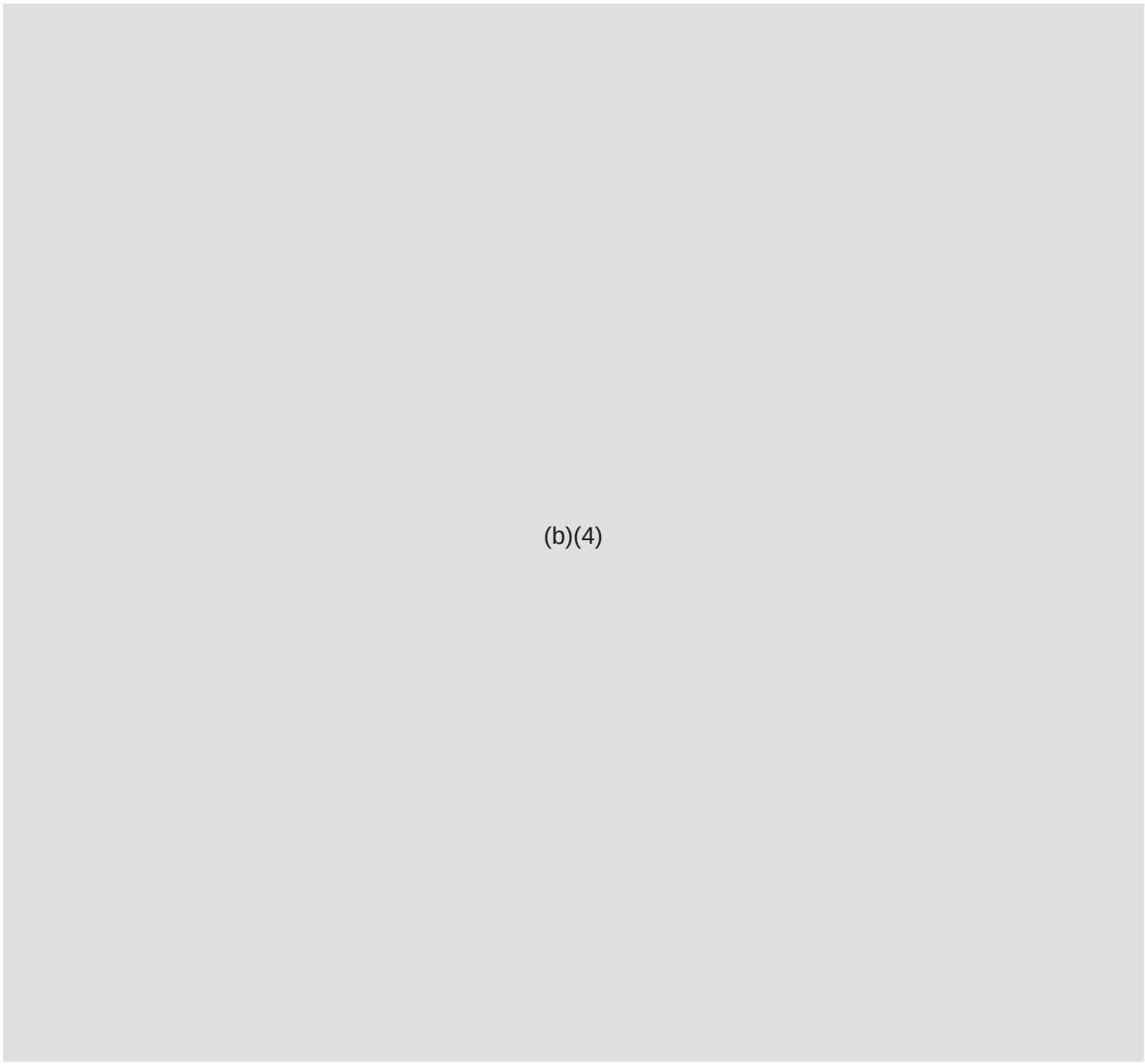
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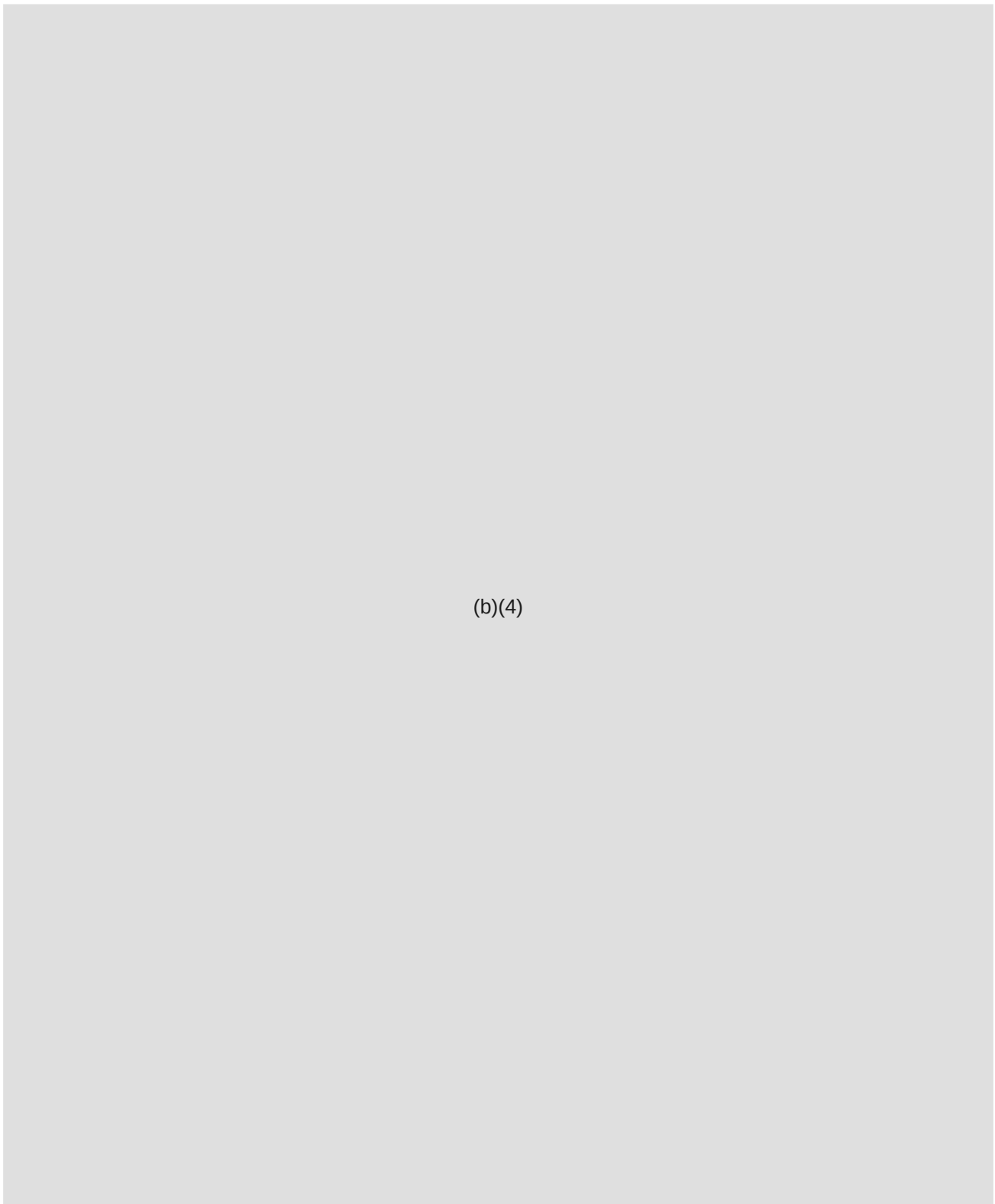
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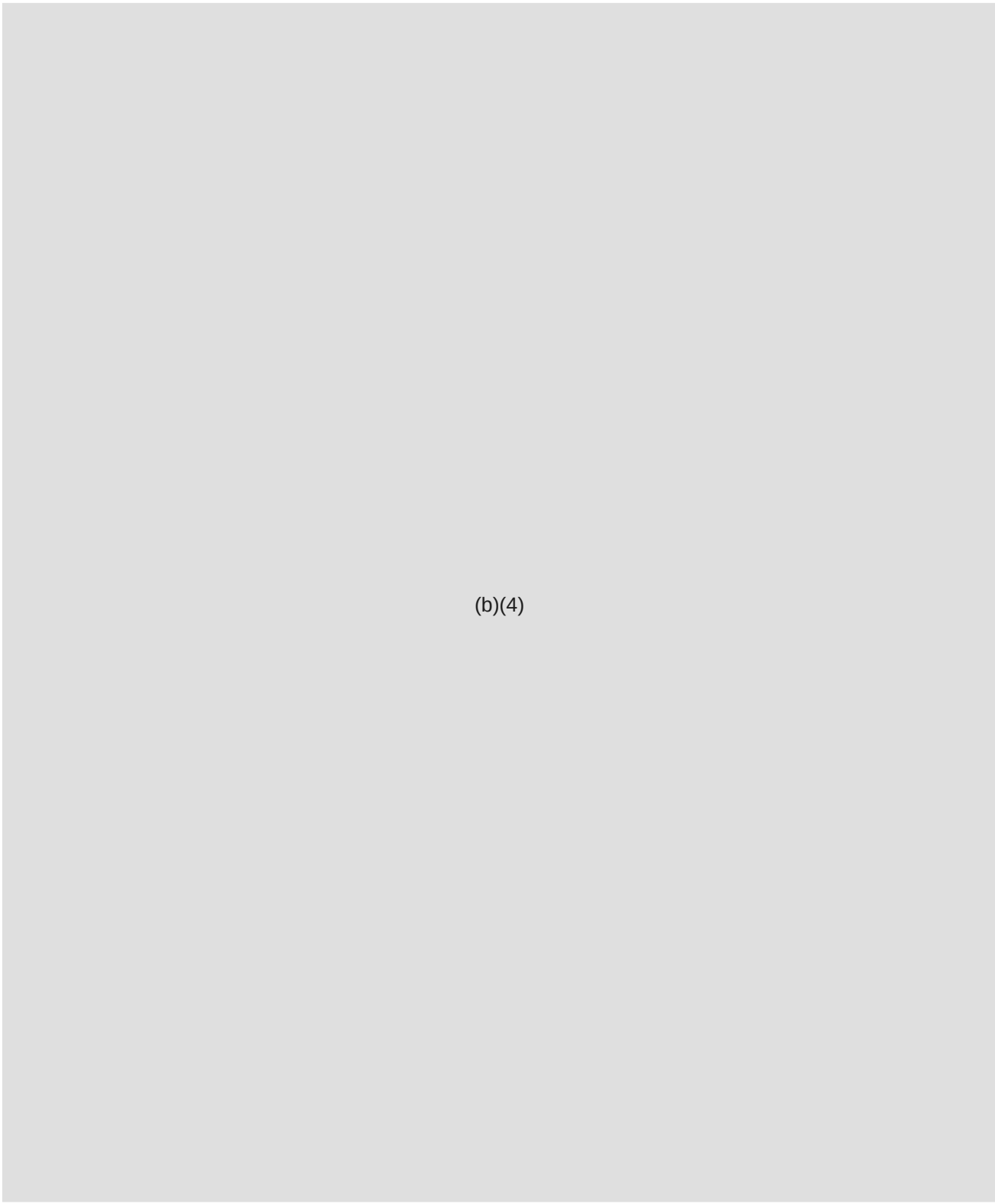
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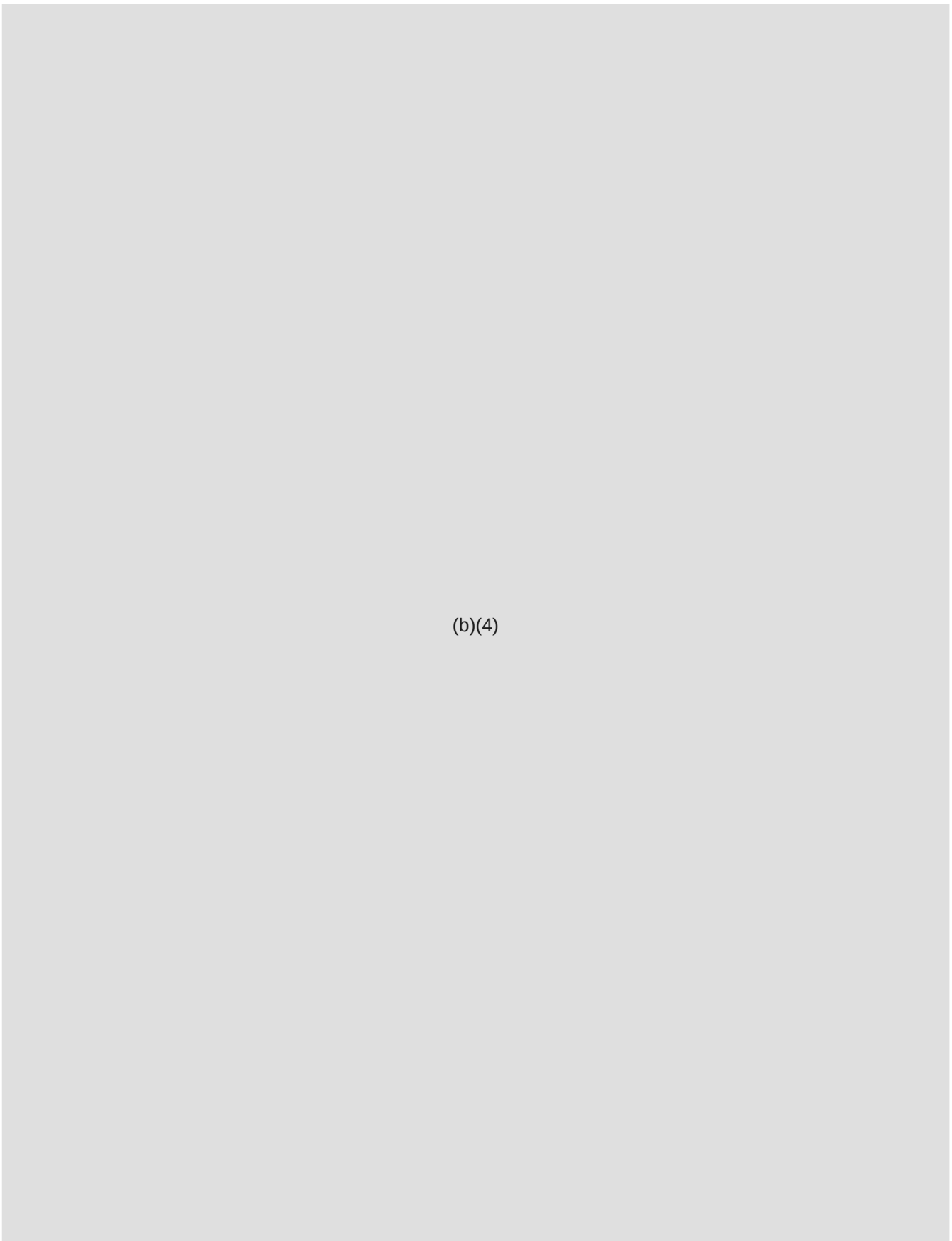
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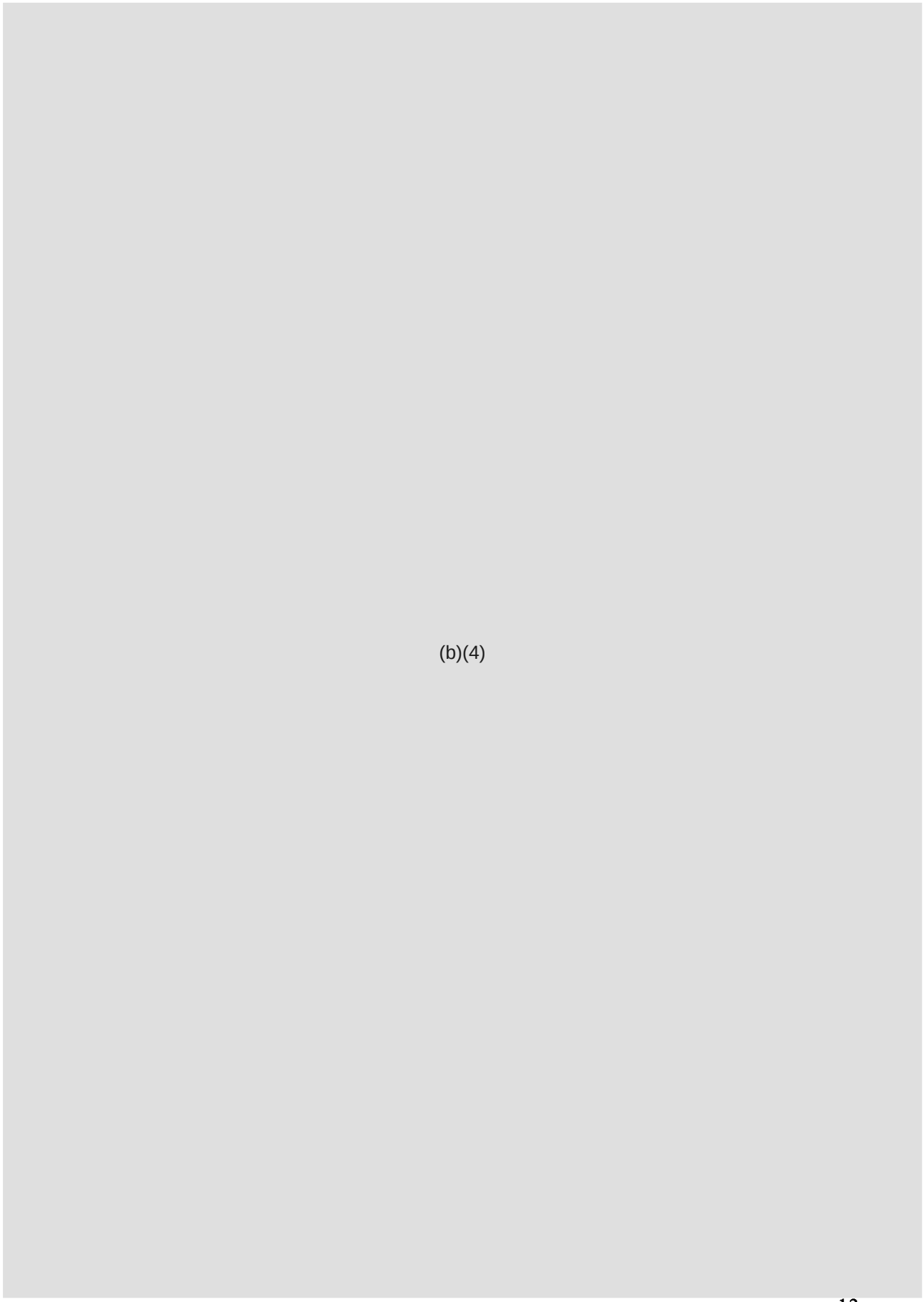
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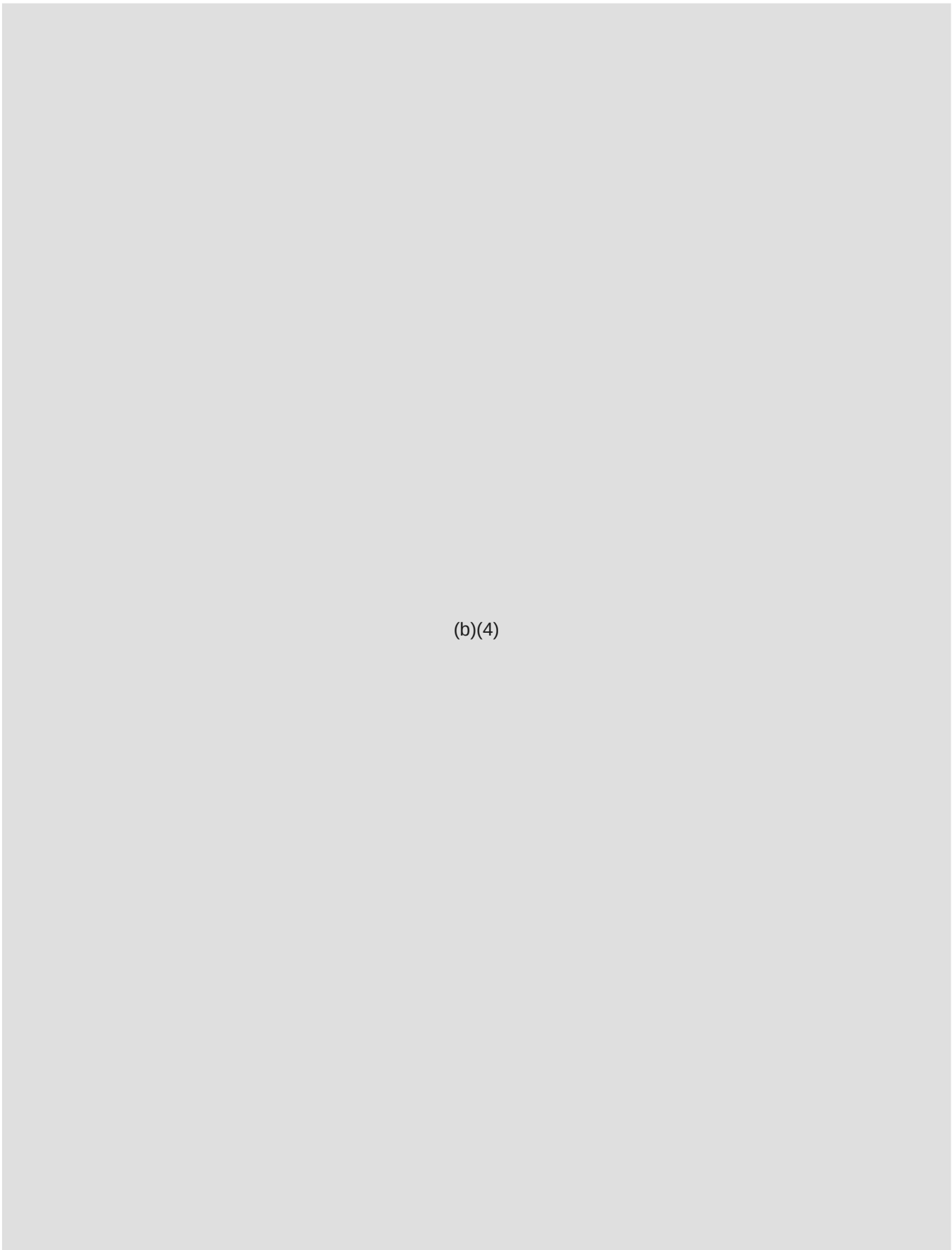
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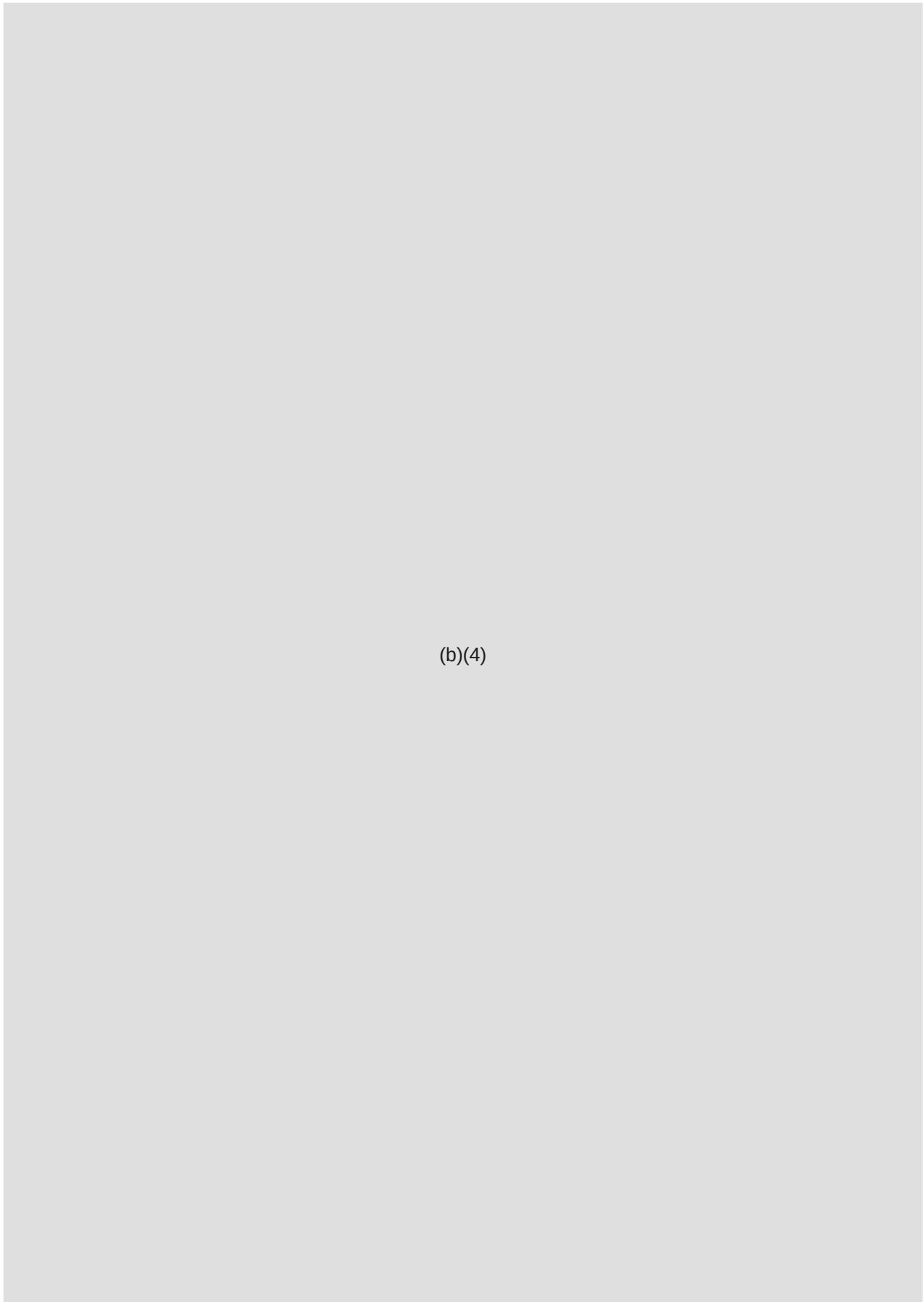
Appendix A – Predictor Analysis Results

This section provides tabular summaries of bilateral placement rates among women in whom bilateral placement was possible (device placed through hysteroscope, no documented PTO, unicornuate uterus or previous tube surgery). In the tables below, NR means "not reported."

Table 9. Success rate by month of Essure procedure.

	Bilateral placement				All
	No		Yes		
	N	%	N	%	N
Date of procedure					
02M03	1	*20.0*	4	*80.0*	5
03M03	.	.	7	*100.0*	7
04M03	1	*7.1*	13	*92.9*	14
05M03	2	*16.7*	10	*83.3*	12
06M03	.	.	29	*100.0*	29
07M03	.	.	29	*100.0*	29
08M03	2	*4.9*	39	*95.1*	41
09M03	1	*4.5*	21	*95.5*	22
10M03	3	*6.1*	46	*93.9*	49
11M03	1	*3.2*	30	*96.8*	31
12M03	2	*5.4*	35	*94.6*	37
01M04	1	*4.0*	24	*96.0*	25
02M04	.	.	21	*100.0*	21
03M04	1	*3.8*	25	*96.2*	26
04M04	.	.	27	*100.0*	27
05M04	1	*4.8*	20	*95.2*	21
06M04	.	.	10	*100.0*	10
07M04	1	*7.7*	12	*92.3*	13
08M04	.	.	20	*100.0*	20
09M04	.	.	15	*100.0*	15
10M04	1	*7.7*	12	*92.3*	13
11M04	.	.	4	*100.0*	4
12M04	1	*25.0*	3	*75.0*	4
01M05	.	.	2	*100.0*	2
Total	19	*4.0*	458	*96.0*	477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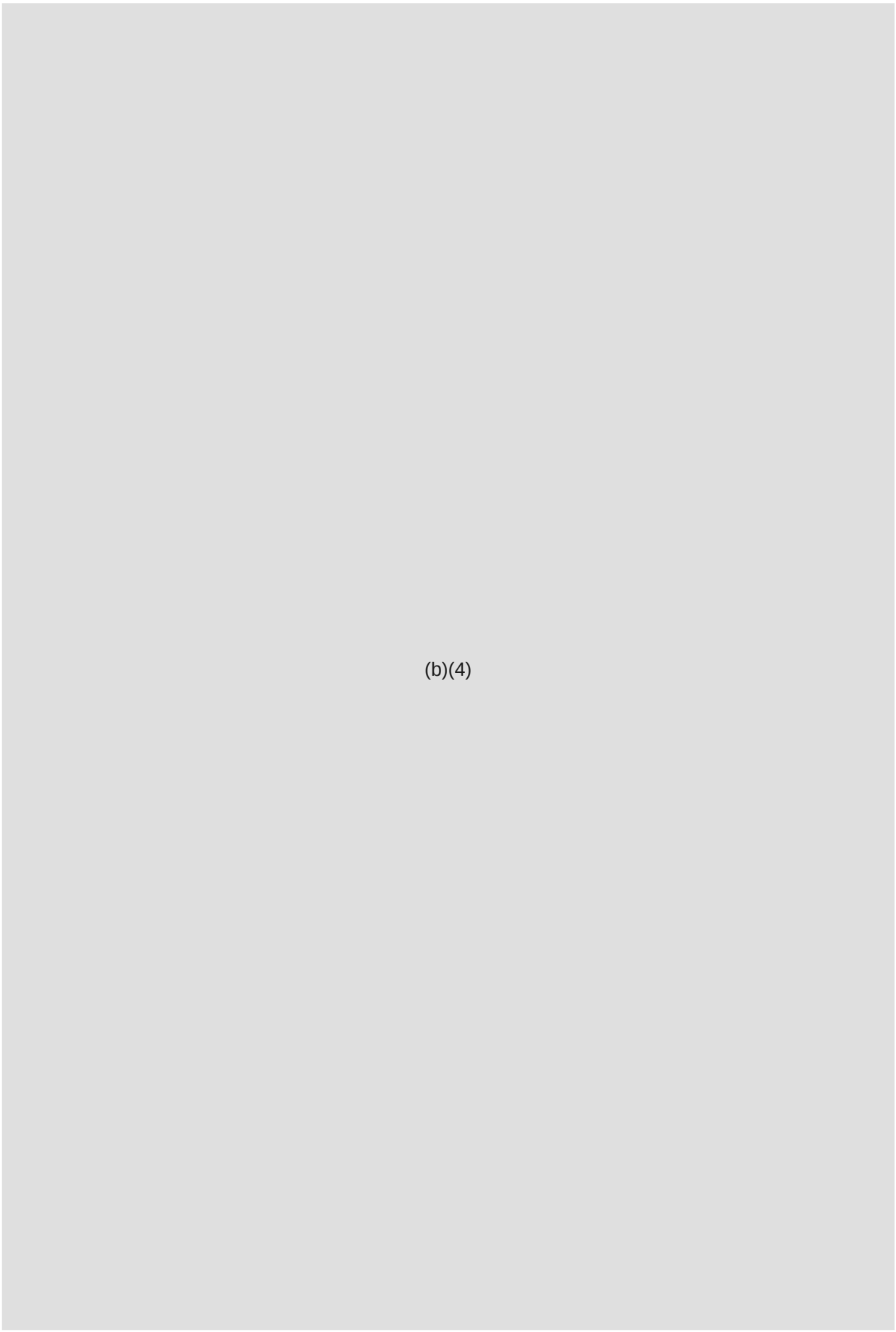
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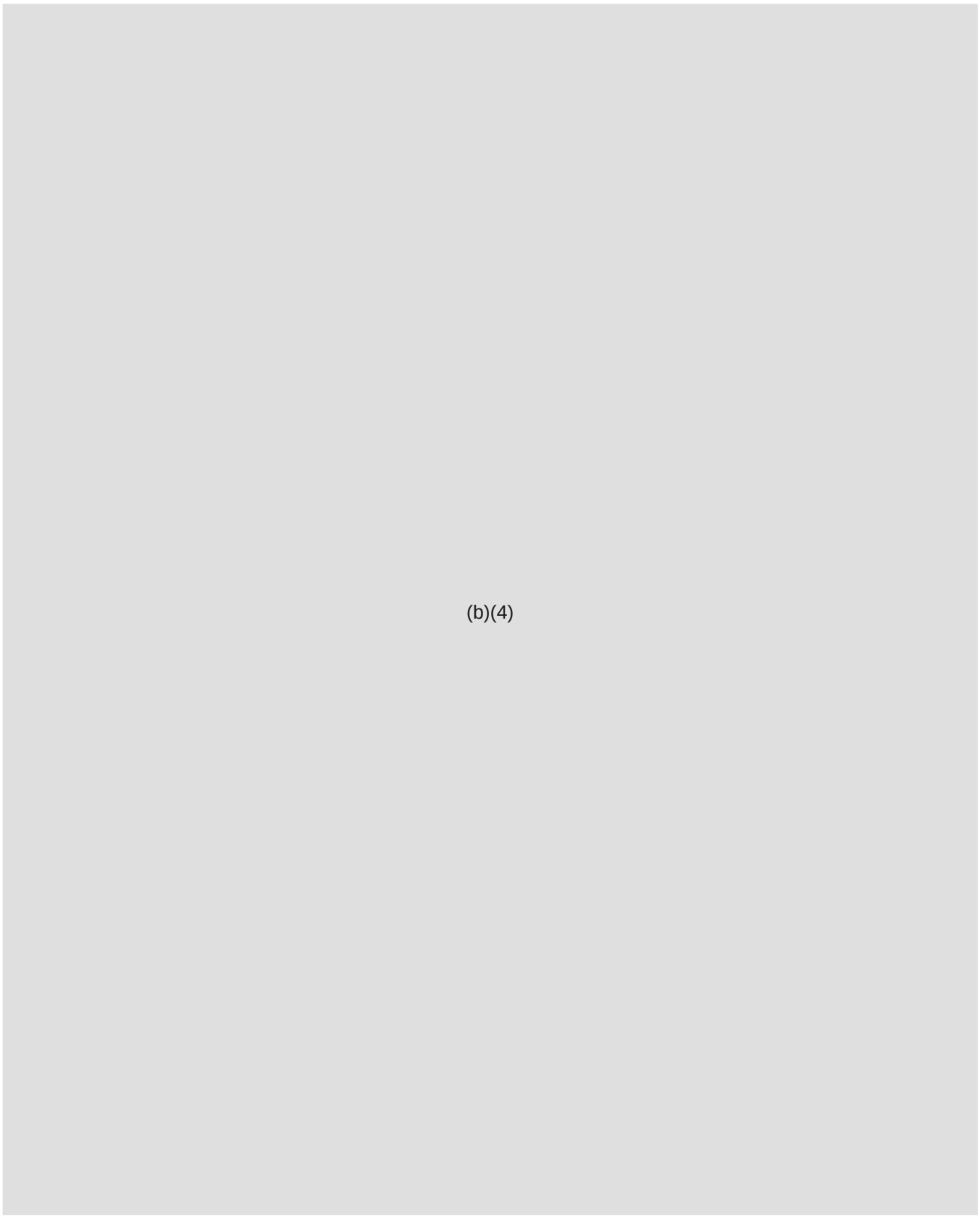
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Exhibit 3

Physician Labeling:
Essure Instructions for Use

C. Potential Adverse Events Not Observed in Clinical Studies

The following adverse events were not experienced by women who participated in clinical studies evaluating the **Essure System** but are still possible:

- Pregnancy and ectopic pregnancy in women relying on **Essure**[2]
- Perforation of internal bodily structures other than the uterus and fallopian tube.
- Adnexal infection/salpingitis.
- Adverse events associated with the hysterosalpingogram or X-rays.
- The effect of future medical procedures that involve the uterus or fallopian tubes on the ability of the **Essure** micro-insert to provide protection against pregnancy.
- Adverse events associated with surgery attempting to reverse the **Essure** procedure, as well as adverse events associated with pregnancy following a reversal procedure or an IVF procedure.
- Adverse events associated with gynecologic surgical procedures (e.g. endometrial ablation).

D. Adverse Event Reporting

Any adverse event (clinical incident) involving the **Essure System** should be reported to Conceptus immediately.

To report an incident, call (877) Essure2 OR 877.377.8732.

IX. CLINICAL STUDIES

A. Purpose of the Study, Study Design, Primary Endpoints

Conceptus has conducted two clinical trials (a Phase II Trial and a Pivotal Trial) to demonstrate the safety and effectiveness of the **Essure System** in providing permanent contraception. Additionally, a third study was performed after pre-marketing approval to evaluate rates of bilateral Essure placement in newly trained physicians.

1. Phase II Study

The Phase II study was a prospective, multi-center, single-arm, non-randomized, international study of women seeking permanent contraception. The objectives of the 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.

[2] One woman in the Phase II study who received a prior device design that was discontinued in 1998 (the Beta design of the STOP device) became pregnant after nearly two years of reliance on the device for contraception. That pregnancy is not included in the effectiveness rate calculations, since that device design was not subject of the Premarket Approval Application (PMA) that supported approval of the **Essure System**.

2. Pivotal Trial

The Pivotal study was a prospective, multi-center, single-arm, non-randomized, international study of women seeking permanent contraception. The study used findings from the U.S. Collaborative Review of Sterilization (CREST study) as a qualitative benchmark. The primary endpoints for the study included:

- Prevention of pregnancy;
- Safety of device placement procedure, and;
- Safety of device wearing.

The secondary endpoints for the study included:

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

3. Post Approval Study for Newly Trained Physicians

The Post Approval Study for Newly Trained Physicians was a prospective, multi-center, single-arm, non-randomized study intended to document the bilateral placement rate for newly trained physicians in the United States. The primary endpoints for the study were:

- Rates of successful bilateral placement of the **Essure System** at first attempt, and;
- Identification of factors predictive of failure to achieve bilateral placement of the **Essure System** at first attempt.

B. Patients Studied

1. The study population of the ~~two~~ Phase II and Pivotal studies combined consisted of (b)(4) women in whom bilateral device placement was achieved after one or more attempts ((b)(4) n the Phase II study and (b)(4) in the Pivotal trial). All study participants were between 21 and 45 years of age and were seeking permanent contraception prior to enrollment in the study. Additionally, all women had at least one live birth, had regular, cyclical menses and were able and willing to use alternative contraception for the first three months following **Essure** micro-insert placement.

2. The study population of the Post Approval Study for Newly Trained Physicians consisted of (b)(4) women in whom micro-insert placement was attempted. A total of (b)(4) nvestigators performed the procedures at (b)(4) JS sites (b)(4) All study participants were between 19 and 49 years of age and were seeking permanent contraception prior to enrollment. Overall, (b)(4) women were considered to have uterine anatomy that, by definition, prevented bilateral placement. This included (b)(4) with unicornuate uterus, (b)(4) with contralateral proximal tubal occlusion, and (b)(4) with known prior tubal surgery. These (b)(4) subjects were

excluded from the adjusted placement rate, thereby reducing the total number of women to (b)(4)

C. Methods

All study participants in the Phase II and Pivotal Trial were screened for eligibility to participate in the clinical study. A complete medical history was obtained. A physical examination, a pelvic examination and required laboratory tests (including a pregnancy test) were conducted.

(b)(4)

(b)(4)

D. Results

Of the (b)(4) women enrolled in the Phase II and Pivotal clinical trials (with bilateral Micro-insert placement) and who have relied on the **Essure System** for contraception for 12 to 36 months, no (zero) pregnancies have been reported. Of the (b)(4) women, (b)(4) have been followed for 12 months, (b)(4) have been followed for 24 months, and (b)(4) have been followed for 36 months. Adverse events that were reported in the clinical studies are provided in Section VIII., B above, and events by study are provided below.

Tables 6 and 7 present the principal safety and effectiveness results and **Tables 8 and 9** present patient demographic information.

Table 6A
Micro-insert Placement and Reliance Rates
in the Phase II and Pivotal Clinical Studies

Outcome	Phase II N=227		Pivotal N=518	
	Number	Percent	Number	Percent
Bilateral Placement*: *After one procedure*	(b)(4)		(b)(4)	
Bilateral Placement*: *After two procedures*				
Reliance Rate*:** *Among women with bilateral placement*				

*The placement rates presented here are based on data from the **Essure** clinical trials. ~~Data on the placement rates in the commercial setting are being gathered in a post-approval study. As updated data regarding placement rates are included in the product labeling, they will also be posted on the Conceptus website: www.Essure.com.~~

**Of these (b)(4) women (b)(4) did not undergo attempted micro-insert placement because the tubal ostia could not be visualized. Also, (b)(4) women who did not achieve bilateral placement underwent a follow-up HSG, and (b)(4) were diagnosed with proximal tubal occlusion (PTO).

***The reliance rate is the number of women who were able to rely on **Essure** for contraception divided by the number of women with bilateral micro-insert placement.

Table 6B
Micro-insert Placement Rate at first attempt in the Commercial Setting

Placement Status	Post Approval Study For Newly Trained Physicians	
	Number	Percent
Bilateral Placement*:	(b)(4)	
Unilateral Placement*:		
No devices placed*:		
Total		

* The placement rates presented here are based on data from the Post Approval Study for Newly Trained Physicians.

(b)(4)

Exhibit 4

Patient Labeling:
Essure Patient Information Booklet

Patient Information Booklet

essure

Permanent Birth Control

Essure: the non-incisional approach to permanent birth control

This booklet is designed to provide important information regarding permanent female contraception (sterilization) using the *Essure* Permanent Birth Control System. This device must be prescribed by a doctor. This booklet is not intended to be a substitute for a thorough discussion with your doctor about whether or not this treatment is right for you. It is important that you read this booklet carefully and discuss its contents with your doctor.

IMPORTANT

This device is intended for permanent pregnancy prevention.

This device does not protect against either HIV infection or other sexually transmitted diseases.

Before this device can be used for contraception, you must first undergo a test, called a hysterosalpingogram (HSG), which is performed to make sure that both of your tubes are blocked and that the devices are in the correct positions. This test is performed approximately 3 months after the *Essure* micro-insert placement procedure. You must use another form of contraception until you have this test and your doctor tells you that you can rely on *Essure* for contraception.

If at any time you suspect that you are pregnant, you should seek immediate medical attention to rule out the possibility that you have an ectopic pregnancy (pregnancy occurring outside of your uterus).

After completion of the *Essure* micro-insert placement procedure, you will be given a patient identification card, which you should keep with you at all times and present to other physicians involved in your present or future care.

Table of Contents

Glossary

Anesthesia—Medically induced partial or complete loss of sensation, in all or part of the body, with or without loss of consciousness. General anesthesia is total loss of consciousness and sensation

Cervix—The passageway that connects the vagina to the uterus

Contraceptive—Any process, device, or method that reduces the likelihood of pregnancy

Delivery Catheter—A long tube-like device that helps the doctor place the *Essure* micro-inserts in the fallopian tubes

Ectopic Pregnancy—The development of a fertilized egg outside of the uterus, but inside the body

Expulsion—Forcing (expelling) something out

Fallopian Tubes—The tubes that carry the eggs from the ovaries to the uterus

Hysterosalpingogram (HSG)—An x-ray of the uterus and fallopian tubes after they have been filled with dye (contrast medium)

Hysteroscope—A telescope-like instrument, which is used to view the inside of the uterus

In Vitro Fertilization (IVF)—Fertilization of an egg outside of the body, followed by placement of the fertilized egg into the uterus

Intrauterine Device (IUD)/Intrauterine System (IUS)—A medical device that is put into the uterus to prevent pregnancy

Irreversible—Cannot be changed back to its original state

Local Anesthetic—Medicine that is applied to or injected in a certain spot in the body to cause a loss of sensation in that part of the body

Major Surgery—Surgery that requires general anesthesia and incisions in the body

Micro-insert—A small, flexible, coil-type device that is put into your fallopian tube for permanent pregnancy prevention

Occlusion—A closed or blocked part of a hollow tube

Perforation—A hole in something

Permanent—Not able to change back and forth

Reversible—Able to change back and forth

Tubal Ligation—Permanent female sterilization by means of cutting, tying, burning, or clipping the fallopian tubes

Uterus—The womb in which a developing fetus grows

Vasectomy—Permanent male sterilization by means of cutting or blocking a segment of the vas deferens (the tube that carries the sperm)

Introducing Essure®

A non-incisional approach to permanent birth control

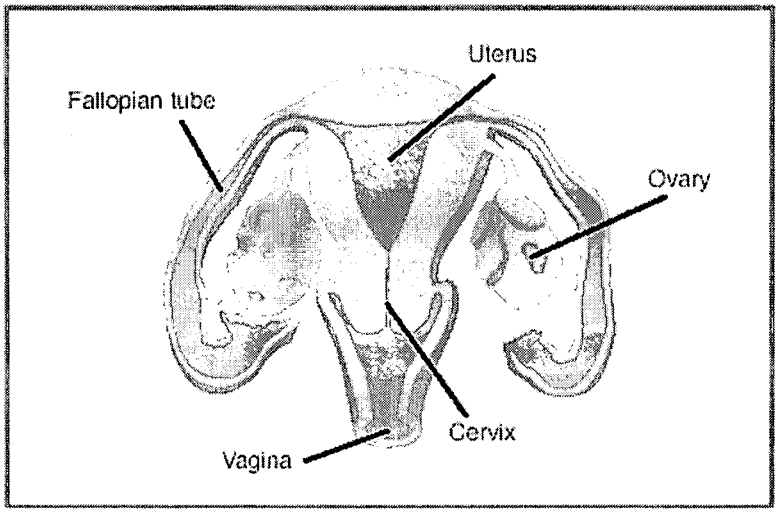
Essure is a new method of permanent birth control developed by Conceptus Incorporated. Because it is intended to permanently prevent pregnancy, it is similar to other permanent birth control procedures, such as vasectomy or tubal ligation ("having your tubes tied"). All of these procedures are intended to prevent pregnancy for the rest of your life.

This brochure will provide you with information about *Essure*, as well as the benefits and risks of this method of birth control; however, this information is not intended to be a substitute for a thorough discussion with your doctor, as all women have individual needs and concerns. Your doctor will advise you whether the *Essure* procedure is appropriate for you with regard to your circumstances and medical history.

How does Essure *work?*

The *Essure* procedure is a non-incisional surgical procedure that involves placing a small, flexible device called a micro-insert into each of your fallopian tubes (the tubes your eggs travel through from your ovaries to your uterus). The micro-inserts are made from polyester fibers and metals (nickel-titanium and stainless steel), materials that have been studied and used in the heart and other parts of the human body for many years.[1] Once the micro-inserts are in place, body tissue grows into the micro-inserts, blocking the fallopian tubes. Blocking the tubes is intended to prevent sperm from reaching and fertilizing the egg, thereby preventing pregnancy. It is believed that the tissue response to the micro-insert that creates the blockage of your tubes will last for the rest of your reproductive life, but data regarding use of *Essure* beyond 3 years are not available. Studies are ongoing to obtain these data. Your doctor will be able to explain the procedure to you in more detail.

The female reproductive organs



What are the benefits of Essure?

Two separate studies of the safety and effectiveness of the *Essure* Permanent Birth Control System have been conducted in women from the United States, Australia, and Europe.[2] The first study involved approximately 200 women, and the second study involved approximately 500 women. The following has been demonstrated in these trials:

No incisions are required[2]

- Unlike the incisional methods of tubal ligation, the *Essure* procedure does not require incisions. It also does not involve cutting, crushing, or burning of the fallopian tubes
- Because there are no incisions, the *Essure* procedure does not cause scars

Can be performed without general anesthesia[2]

- The *Essure* procedure can be performed without general anesthesia. In the clinical trials of *Essure*, general anesthesia was used rarely

Essure *does not contain hormones*[2]

- The *Essure* micro-inserts do not contain or release any hormones

Effective[2]

- In the first study, 192 women relied on *Essure* for contraception for 1 year, 177 relied on *Essure* for contraception for 2 years, and 172 relied on *Essure* for contraception for 3 years. In the second study, 434 women relied on *Essure* for contraception for 1 year, 403 relied on *Essure* for contraception for 2 years, and 21 for 3 years. None of the women who relied on *Essure* for contraception during the clinical trials became pregnant over the 1 to 3 years of follow-up. However, no method of contraception is 100% effective, and there is a small chance that you can become pregnant.[3] Additional information regarding the effectiveness of *Essure* and other methods of contraception is found in Tables 1 and 2.

Rapid recovery[2]

- The procedure time to place the *Essure* micro-inserts averaged 35 minutes. Women were typically discharged from the medical facility after waiting an additional 45 minutes after the placement procedure was complete
- Almost all employed women who participated in the second *Essure* study resumed work in 24 hours or less after the day of the procedure. Return to work was not evaluated in the first study
- The majority of women returned to normal activities in 1 to 2 days
- Almost all women rated their comfort as "good" to "excellent" within 1 week of the procedure

High patient satisfaction[2]

- Women in the Pivotal Study consistently rated their overall satisfaction with the *Essure* micro-inserts as very high

The Essure® procedure: key risks and considerations

The procedure should be considered irreversible

There are no data on the safety or effectiveness of surgery to reverse the *Essure* procedure. What is known is that any attempt to surgically reverse the *Essure* procedure will require major surgery and has a poor chance for success. *Essure* is only meant to be used by women who are certain they no longer want to have children. There are also no data on the safety or effectiveness of in vitro fertilization (IVF) after the *Essure* procedure has been performed.

Studies have shown that women under the age of 30 are more likely to **regret their decision to be sterilized.**[4] If you are under 30 years old, this decision should be considered carefully, especially since the *Essure* procedure should not be considered reversible at any age.

Like all methods of birth control, the Essure *procedure should not be considered 100% effective*

No method of birth control is 100% effective, and there is a small chance you can become pregnant, even many years after you undergo the procedure. The risk of unintended pregnancy, even years after the procedure, also exists for patients who chose incisional tubal ligation or vasectomy.[3] Also, because any type of tubal ligation affects the fallopian tube, where a pregnancy begins before it moves into the uterus, there is an increased risk of a tubal pregnancy (ectopic pregnancy occurring in the fallopian tube), should you become pregnant.[5]

Not all women who undergo the Essure *placement procedure will achieve successful placement of both micro-inserts*

Approximately 1 out of every ~~7~~ 25 women ~~in the *Essure* clinical studies~~ did not achieve successful placement of both micro-inserts during the first placement procedure in an *Essure* clinical study performed in the commercial setting.[2] In previous *Essure* clinical trials, ~~Some~~ some ~~of these~~ women also did not achieve successful placement of both micro-inserts during the first placement procedure and chose to undergo a second placement procedure.~~,~~ They achieved successful placement of both micro-inserts during the second procedure, and subsequently were able to rely on *Essure* for contraception.[2]

If you do not receive successful placement of both micro-inserts during the first procedure, you should talk with your doctor about whether to undergo a second placement procedure or to rely on other methods of birth control.

You must use another method of birth control for at least 3 months after the procedure

It takes at least 3 months before your doctor can advise you whether you can begin relying on *Essure* for contraception. You will need to visit your doctor 3 months after your *Essure* procedure to have an evaluation performed. This evaluation is called a hysterosalpingogram (HSG), and it is performed to make sure that both of your *Essure* micro-inserts are in the correct location and that

both of your tubes have been blocked. The HSG involves injection of contrast (dye) into your uterus so that an x-ray can be taken. It is important that you do not rely on *Essure* for contraception until your doctor has performed this test and has told you that you may rely on *Essure* for contraception. If you rely on *Essure* for contraception before completing this evaluation, you may get pregnant or have an ectopic pregnancy (pregnancy outside of your uterus). Ectopic pregnancies can be life threatening. Because of this 3-month waiting period, you will need to talk to your doctor (before the procedure is performed) about another contraceptive method to use with *Essure* during this time. During this 3-month period, intrauterine devices (IUDs) and intrauterine systems (IUSs) cannot be used.

The Essure *procedure is newer than other procedures*

Essure is one of the newest methods of permanent birth control, so it has not been studied in as many women or for as long as most birth control methods. Over 600 clinical study participants have relied on *Essure* for contraception for 1 year, approximately 580 of them have relied on *Essure* for 2 years, and approximately 190 women have relied on *Essure* for 3 years.[2] There are very little data on the safety of or the chance of pregnancy with *Essure* beyond this time frame. Once longer-term data are available, the information on the safety of and chance of getting pregnant while using *Essure* may be different than the data based on 1 to 3 years of use.

Removal of the Essure *micro-inserts requires surgery*

If the *Essure* micro-inserts need to be removed for any reason after they have been placed in your body, major surgery will be required. This surgery will require an abdominal incision and, most likely, general anesthesia.

As with all procedures, there are risks associated with Essure

You should be aware of these risks and discuss them in detail with your doctor before you make your decision. Some of the risks associated with *Essure* have already been discussed above, but additional risks, such as pain and bleeding following the *Essure* placement procedure as well as risks associated with future medical procedures that you may undergo after your *Essure* placement procedure, are discussed in the *Risks* section at the end of this booklet. Please read the *Risks* section at the end of this booklet carefully. In addition to the risks previously discussed, other risks and considerations are also discussed. Some of the risks discussed in this booklet were experienced by women in the clinical studies of *Essure*. Some of the risks were not among those reported during the clinical trials, but should still be considered as potential risks of *Essure*. You should talk to your doctor about the likelihood of these risks, particularly in relation to your own situation.

Is Essure® right for you?

The *Essure* procedure is only appropriate if you are sure you do not want any more children, would like to have permanent birth control, and believe you will not change your mind. If there is any chance you may want to have children in the future, you should choose another form of birth control. You should avoid making this choice during times of stress, such as a divorce or after a miscarriage, and NEVER while under or due to pressure from a partner or others.

YOU SHOULD NOT USE the Essure *Permanent Birth Control System if you:*

- Are uncertain about your desire to end fertility
- Are pregnant or suspect that you are pregnant
- Have delivered a baby, had a miscarriage, or had an abortion within 6 weeks before the *Essure* micro-insert placement procedure
- Have an active or recent pelvic infection
- Have an unusual uterine shape (for example, a uterus with only one tube or a divided uterus)
- Have a known allergy to dye (contrast media)
- Have a known hypersensitivity or allergy to nickel as confirmed by skin test
- Are unwilling to use another method of contraception for at least 3 months after the *Essure* micro-insert placement procedure
- Are unwilling to undergo an HSG approximately 3 months after your *Essure* placement procedure to make sure that your tubes are blocked and the devices are in the correct positions
- Have had a prior tubal ligation

Note: If you are currently undergoing immunosuppressive therapy (eg, taking steroid medication such as prednisone, undergoing chemotherapy, etc), you should discuss this in detail with your physician, since the *Essure* micro-inserts may not be effective in patients undergoing immunosuppressive therapy. Also, if you have previously had abdominal or pelvic surgery, please discuss this with your physician prior to undergoing an *Essure* placement procedure.

If you decide you want to have the *Essure* procedure performed, you will undergo a general examination and laboratory tests (for example, a PAP smear) to evaluate whether you are a good candidate for the procedure. It may turn out that the *Essure* procedure is not an option for you.

You should be aware that there are other methods of birth control, both temporary/reversible and permanent. **Table 1** on the following page shows pregnancy rates for various birth control methods. This information is being presented to assist you in your choice of contraception during the 3-month waiting period until the HSG is performed after placement of the *Essure* micro-inserts. **Table 2** provides information regarding some of the characteristics of the 3 forms of permanent birth control: *Essure*, tubal ligation, and vasectomy. Your doctor will explain these alternative methods to you and advise you whether *Essure* is a suitable option for you. It is your right to decide what method suits you. If, at any time before the start of the *Essure* procedure, you decide not to have it, you should tell your doctor and cancel the procedure. You do not have to provide any explanation or reason for your decision.

Table 1 Pregnancy Rates for Temporary Birth Control Methods[3,6-8,*]

(For 1 Year of Use).

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for 1 year. These estimates are based on a variety of studies.

Method	Rate of Pregnancy
Hormonal Methods:	
Implant (Norplant® [levonorgestrel implants] and Norplant® 2 [levonorgestrel implants])	0.05%
Hormone Shot (Depo-Provera® [medroxyprogesterone acetate injectable suspension])	0.3%
Combined Pill (Estrogen/Progestin)	5%
Minipill (Progestin only)	5%
NuvaRing® (etonogestrel/ethinyl estradiol vaginal ring)	1.2%
Ortho Evra™ (norelgestromin/ethinyl estradiol transdermal system)	1%
Lunelle™ (medroxyprogesterone acetate and estradiol cypionate injectable suspension)	<1%
Barrier Methods:	
Male Latex Condom†	14%
Diaphragm†	17%
Cervical Cap†	17%
Female Condom	21%
Lea's Shield®	15%
Spermicide:	
Gel, Foam, Suppository, Film	26%
Natural Methods:	
Withdrawal	19%
Natural Family Planning (calendar, temperature, cervical mucus)	25%
No Method	85%

*Data adapted from FDA's Uniform Contraceptive Table and modified per FDA input based on new studies.

†Used without spermicide.

‡Used with spermicide.

Please note that information regarding the failure rates with IUDs and IUSs is not presented since these methods of birth control cannot be used during the 3-month waiting period after the Essure placement procedure.

Table 2 Permanent Methods of Birth Control[2,3,5,9,10]

The following table provides information about the permanent birth control methods currently available: *Essure*, tubal ligation, and vasectomy.[2,3,5,9,10]

	Essure®
Who undergoes the procedure?	Women
How effective is the procedure?	The estimates of effectiveness (no pregnancy) are: 99.93% at 1 year of follow-up. 99.86% at 2 years of follow-up. 99.80% at 3 years of follow-up. Data not available beyond 3 years.
How is the surgical procedure performed?	The devices are routed through the vagina, cervix, and uterus into the fallopian tubes, where the devices are placed. No incisions are required.
How long does the procedure take?	Average procedure time is 35 minutes.
How many visits to the doctor does it require, and what type of follow-up is required?	Three visits. One consultation visit, 1 visit to place the micro-inserts, and 1 follow-up visit at 3 months to check for tubal occlusion and proper micro-insert location.
How is pain or discomfort controlled during the procedure?	Local anesthetic and/or intravenous sedation.
Can I rely on it right away?	No. There is a 3-month waiting period, during which another form of contraception must be used. You will need a hysterosalpingogram (HSG [a special kind of x-ray]) before you can rely on *Essure*. The purpose of this test is to make sure that both of the tubes are blocked and both of your devices are in the correct position. You must continue to use another form of contraception until your doctor instructs you that you can rely on *Essure* for birth control.

	Tubal Ligation	Vasectomy
	Women	Men
	99.45% at 1 year of follow-up. 99.16% at 2 years of follow-up. 99.15% at 10 years of follow-up.	99.85% at 1 year of follow-up.
	The fallopian tubes are either cut, burned (cauterized), or clamped using either: • Laparoscopic tubal ligation (most common method), where 1 to 2 incisions are made in the abdomen to access the fallopian tubes using a telescope-type device. The tubes are then blocked with clips or rings or burned • Open surgery (called a laparotomy or mini-laparotomy), which requires a larger incision (usually 2 to 5 cm) in the abdomen	The 2 tubes (the vas deferens) that carry sperm from the testicles to the penis are cut or blocked. This is achieved by: • Making a small incision in the scrotum. This is the most common method • Making a small puncture in the center of the scrotum
	Average procedure time is 30 to 45 minutes for laparoscopic method. May be longer if open surgery.	Average procedure time is 15 to 30 minutes.
	Three visits. One consultation visit, 1 visit to perform the tubal ligation, and 1 follow-up visit in 1 to 2 weeks to check the incisions.	Three visits. One consultation visit, 1 visit to perform the vasectomy, and 1 follow-up visit to make sure that the vasectomy is effective (ie, sperm count is 0).
	General anesthetic, spinal block, or epidural anesthesia is typically used.	Local or general anesthetic.
	Yes. Following your doctor's advice, you may resume intercourse when you have recovered from the procedure, typically about a week after the procedure.	No. There is a 2 to 3 month waiting period required to flush out any existing sperm. Sperm counts are taken to demonstrate the success of vasectomy, ie, when the sperm count is 0. You must use another method of contraception until then.

Table 2 Permanent Methods of Birth Control[2,3,5,9,10] (continued)

	Essure®
What should I be doing to help the recovery process after the procedure?	• Rest for 45 minutes following the procedure before going home. Follow your doctor's instructions to report any unusual pain, bleeding, or high fever • Consider having someone drive you home
When can I return to regular activities?	Typically, within 1 to 2 days of the procedure.
What are the typical temporary effects following the procedure?	• Cramps (like menstrual cramps) • Discharge (like a light menstrual flow or spotting) • Mild nausea or vomiting associated with the procedure • Fainting or lightheadedness following the procedure
What are the major risks of the procedure?	• You may become pregnant several years after undergoing the procedure • Ectopic pregnancy occurs more often in women who have had a sterilization, if they become pregnant • For a percentage of women (14% in the ~~clinical studies~~) it may not be ~~possible~~ to place the micro-inserts in the fallopian tubes during the first placement procedure • Despite micro-insert placement, a small percentage of women (3% in the clinical studies) may not be able to rely on the micro-inserts for birth control due to incorrect position of the devices or lack of tubal blockage • Although death and serious injury following hypervolemia were not reported in the *Essure* clinical trials, hypervolemia can lead to serious injury and death

(4% in the commercial study)

Tubal Ligation	Vasectomy
• Most women are ready to go home 2 to 4 hours after the procedure • Must have someone drive you home • The incision will need to be kept dry for a few days • Follow your doctor's instructions to report any unusual pain, bleeding, or high fever	• Rest for at least 15 minutes following surgery • Consider having someone drive you home • Apply ice packs to the scrotum and wear supportive underwear to minimize bruising/swelling • Follow your doctor's instructions to report any unusual pain, bleeding, or high fever
For laparoscopic tubal ligation, typically within 4 to 6 days. For tubal ligation performed by an open procedure, typically within 9 to 10 days.	Typically, in 2 days.
• Cramps (like menstrual cramps) • Discharge (like a menstrual flow) • Mild nausea or vomiting associated with general anesthesia or the procedure • Pain in the neck or shoulder • Pain in the incision • A scratchy throat if a breathing tube was used • Feeling tired and achy • Swollen abdomen, which resolves as gases are absorbed • Bruising around the incision that fades	• Swelling and bruising. If this occurs, it usually resolves within 2 weeks following the procedure • A dull ache in the testicles that usually fades during the first week
• You may become pregnant several years after undergoing the procedure • Ectopic pregnancy occurs more often in women who have had a sterilization, if they become pregnant • Major complications, such as infections, bowel injuries, bleeding, burns, or complications from anesthesia, occur in about 2% of women who have the operation by laparoscopy and in about 6% of women who have the operation by laparotomy (open procedure). Internal bleeding is the most common and may require an open operation to stop the bleeding • Other injuries such as damage to the bladder or burns to the bowel may also require additional surgery • Other risks such as blood clots and death are rare	• Pregnancy may occur several years after undergoing the procedure • Bruising on the scrotum is experienced by 1.6% of men • Infection of the incision/puncture in the scrotum is experienced by 1.5% of men • Painful testicles (epididymitis) is experienced by about 1.4% of men • Sperm may leak into the surrounding tissue (less than 1% leakage rate) forming small lumps (granuloma). This process generally subsides spontaneously, although pain medication may be required

Risks

Failure to place 1 or both of the Essure® *micro-inserts in the correct location or to obtain tubal occlusion by 3 months after the procedure*[2]

In the ~~clinical studies~~commercial study, approximately 1 out of every ~~7~~ 25 women were not able to have the microinserts placed in both fallopian tubes during the first placement procedure. In previous clinical studies ~~At~~ at routine 3-month follow-up, 4% of the women who did receive placement in both tubes were found to have micro-inserts in the incorrect position. The types of incorrect positions included:

- The micro-insert(s) was (were) too far or not far enough into the tube
- The micro-insert(s) had been poked through the wall of the fallopian tube or uterus (perforation)
- The micro-insert(s) had come out of the body (expulsion)
- The micro-insert(s) was (were) in the body, but outside the fallopian tube

As a result of the above-listed incorrect positions of the micro-insert(s), these women could not *initially* rely on the *Essure* micro-inserts for birth control. Some of the women whose micro-inserts had come out of their bodies decided to undergo a second placement procedure and were then able to rely on the micro-inserts for birth control.

Approximately 3.5% of women did not have occlusion of both fallopian tubes at the HSG performed 3 months after the procedure. All of the women, however, did have occlusion of both fallopian tubes at a second HSG performed approximately 6 months after the procedure.

A very small percentage of women in the *Essure* clinical trials (1.8%) were identified as having tubal perforations related to placement of the *Essure* micro-inserts. Most of these women underwent laparoscopic sterilization and about half of the women had the devices retrieved. Therefore, if it is necessary to retrieve *Essure* micro-inserts that perforate the uterus or fallopian tubes, laparoscopy or other surgical methods will be required. In the event of tubal perforation, an alternate tubal sterilization procedure may be needed for women desiring permanent contraception.

Other complications that can occur during the Essure *placement procedure and postprocedure recovery*[2]

- Pain/vaginal bleeding. Most women in the clinical studies reported mild to moderate pain during the *Essure* micro-insert placement procedure. Many women reported mild to moderate pain and/or cramping and vaginal bleeding for a few days following the procedure

- Nausea/vomiting/fainting. Some women in the clinical studies reported nausea and/or vomiting or fainting following the procedure

- Overabsorption of fluid. Rarely, women in the clinical studies absorbed too much of the fluid used to expand the uterus during the placement procedure. This can result in shortness of breath or the need for medication to get rid of the excess fluid. If this condition is not treated by your doctor immediately, serious complications can occur, including death

- Broken *Essure* micro-insert. Rarely in the clinical studies, a portion of the *Essure* micro-insert was broken off during the placement procedure. This occurrence has not been reported to have caused a problem in preventing pregnancy or to have resulted in pain or other problems

- Undiagnosed pregnancy at time of *Essure* placement procedure. Women who undergo the *Essure* placement procedure, or any other sterilization procedure, during the second half of their menstrual cycle (after ovulation) are at an increased risk of unknowingly being pregnant at the time of the placement procedure. Therefore, the micro-insert placement procedure should be scheduled during the first half of the menstrual cycle, before ovulation occurs. On rare occasions during the clinical studies, when the *Essure* procedure was performed in the second half of the menstrual cycle, the women in whom the procedure was performed were unknowingly pregnant at the time of the procedure. The effects of the micro-inserts on you or the developing fetus are not known

- Anesthesia risks. There are risks associated with the anesthesia (medicine to control sensation or consciousness) used during the *Essure* placement procedure. You should discuss with your doctor the risks of the particular anesthesia method recommended for you

- Infection. You should contact your doctor if you have fever, vaginal discharge or odor, or severe pain following the procedure

Risks (continued)

Complications that may occur after the Essure® *placement procedure*

- Pregnancy. No method of birth control is 100% effective, so pregnancy can occur even with a permanent birth control procedure such as *Essure*. *Essure* has been demonstrated in clinical studies to be 99.80% effective at 3 years of follow-up[2]

- *Ectopic* pregnancy. Ectopic pregnancy is when the pregnancy occurs outside of the uterus (womb), usually in one of the fallopian tubes. While this did not occur in the clinical studies, it is still possible with the *Essure* procedure. Women who undergo sterilization, by *Essure* or incisional tubal ligation, are more likely to have an ectopic pregnancy if they get pregnant. If your period is more than 5 days late, or you suspect for any reason that you might be pregnant, call your doctor immediately so that you can be tested for pregnancy and monitored for the possibility of ectopic pregnancy. Ectopic pregnancy can be life threatening if not treated

- Risks to mother/fetus if you become pregnant. If you do become pregnant, the risk of the *Essure* micro-inserts to you, the continuation of the pregnancy, the fetus, childbirth, or a pregnancy termination procedure (abortion) are unknown

- Changes in menstrual cycle (period). Some women in the clinical studies reported temporary changes in their periods; however, very few women reported permanent changes. These temporary/permanent changes included the following:
  —periods that were heavier or longer than normal
  —bleeding or spotting between periods

- Pelvic/back/abdominal pain. Some women in the clinical studies reported 1 or more episodes of pelvic, back, or abdominal pain. Very few women reported persistent pain

- Regret. As with any major decision, there is the risk that you will regret your decision to end your fertility. The risk is much greater for younger women

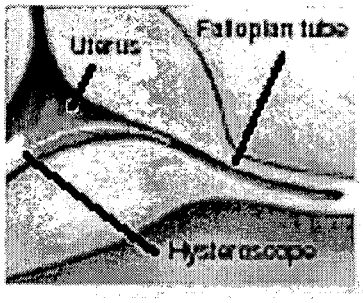
- Pelvic inflammatory disease. If an infection occurs, there is the potential for pelvic inflammatory disease. This was not reported during the clinical trials

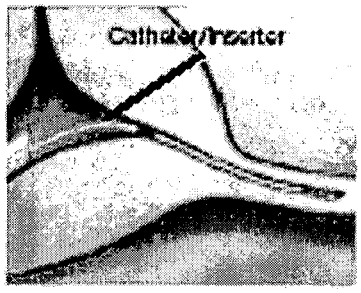
- Risks of hysterosalpingogram (HSG)/x-ray. There are risks associated with the HSG that is performed before you can rely on *Essure* for contraception. You should discuss these risks with your doctor

- Risks of future medical procedures. In the future, you may be offered or require medical procedures that involve the uterus or fallopian tubes. The safety and effectiveness of these procedures, such as those identified below, in women who have the *Essure* micro-inserts are not known. In addition, such procedures could interrupt the ability of the *Essure* micro-inserts to prevent pregnancy. Whenever you have any medical procedure or see a new doctor, tell the doctor that you have this device. Some of the procedures that can involve possible risks are:
  - dilation and curettage of the uterus (D&C) or endometrial biopsy, because these methods may snag the portion of the micro-insert that is in the uterus
  - hysteroscopy or endometrial ablation, because these methods sometimes use electrical energy, which may heat the micro-inserts and cause tissue damage
  - in vitro fertilization (IVF), because this method may snag the portion of the micro-insert that is in the uterus or the micro-inserts may interfere with successful implantation of the fertilized egg. There are no data on the safety or effectiveness of IVF with *Essure*. If pregnancy is achieved, the risks of the micro-inserts to your health, the continuation of the pregnancy, the fetus, or childbirth are unknown

- Magnetic resonance imaging (MRI). The *Essure* micro-inserts were found to be safe at a high MRI field strength. However, when undergoing MRI, the presence of the micro-inserts can produce an obscure image of tissue at or near the micro-inserts.[2] Whenever you have a medical procedure or see a new doctor, tell the doctor that you have this device and show your patient identification card to your doctor

How is the Essure® procedure performed?





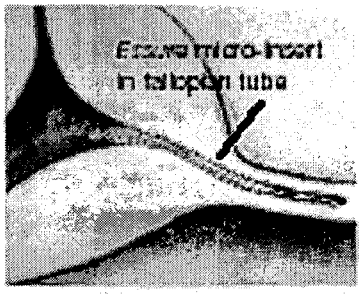
One to 2 hours before the procedure, you are given medication to reduce tubal spasms and uterine cramping during the procedure.

Step 1

After a local anesthetic is injected into or applied to the cervix, the doctor inserts a narrow telescope, called a hysteroscope, through your vagina and cervix (the entrance to the uterus from the vagina) and into the uterus. The doctor may need to gently expand the opening of your cervix and may insert an instrument to do this. The hysteroscope is attached to a video camera and monitor so the doctor is able to see exactly what he or she is doing. Fluid, called normal saline (salt water), flows through the hysteroscope and into your uterus. The fluid is used to expand the uterus so the doctor can see the openings to your fallopian tubes. You might feel cramping from this.

Step 2

A narrow inserter, called a catheter, is passed through the hysteroscope and into your fallopian tube. The micro-insert is attached to the end of the inserter.



Step 3

The micro-insert is placed in the fallopian tube and the inserter is removed. The process is repeated in the other fallopian tube. The entire procedure should take about 35 minutes, with only 15 minutes typically required to place the micro-inserts into the fallopian tubes.

Step 4

During the next 3 months, tissue will begin to grow into the micro-inserts, eventually blocking your fallopian tubes. You will need to use another form of birth control during this period until your doctor confirms that the procedure has worked.

After 3 months, you need to have a test called a hysterosalpingogram (HSG). This test is required before your doctor can tell you whether you may begin relying on *Essure* for contraception. During an HSG, your doctor fills your uterus with dye and then takes an x-ray to see if the dye remained in your uterus or traveled down your fallopian tubes. The purpose of this test is to make sure that both of your tubes are blocked and that both of the micro-inserts are in the correct position.

Note: Always call your doctor if you have any unusual pain, bleeding, or other symptoms.

www.essure.com

1-877-ESSURE1 (1-877-377-8731) Essure Information Center

For more information on the *Essure*® procedure, please speak to your doctor.

References: **1.** Valle RF, Carignan CS, Wright TC, and the STOP Prehysterectomy Investigation Group. Tissue response to the STOP microcoil transcervical permanent contraceptive device: results from a prehysterectomy study. *Fert Steril.* 2001;76:974-980. **2.** Data on file, Essure PMA Submission, October 2002, and Supplements, Conceptus Incorporated. **3.** Hatcher RA, Trussell J, Stewart F, et al. *Contraceptive Technology.* 17th rev ed. New York, NY: Ardent Media; 1998. **4.** Wilcox LS, Zeger SL, Chu SY, Peterson HB, Baker ED. Risk factors for regret after tubal sterilization: 5 years of follow-up in a prospective study. *Fert Steril.* 1991;55:927-933. **5.** American College of Obstetricians and Gynecologists (ACOG). Sterilization by Laparoscopy. Patient Education Brochure, AP035; April 2000. **6.** Organon Inc. NuvaRing. Available at: www.nuvaring.com. Accessed November 8, 2002. **7.** Ortho-McNeil Pharmaceutical. Ortho Evra. Available at: www.orthoevra.com. Accessed November 8, 2002. **8.** Pharmacia Corporation. Lunelle. Available at: www.lunelle.com. Accessed November 8, 2002. **9.** Jamieson DJ, Hills SD, Duerr A, Marchbanks PA, Costello C, Peterson HB, for the U.S. Collaborative Review of Sterilization Working Group. Complications of interval laparoscopic tubal sterilization: findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol.* 2000;96:997-1002. **10.** Layde PM, Peterson HB, Dicker RC, DeStefano F, Rubin GL, Ory HW. Risk factors for complications of interval tubal sterilization by laparotomy. *Obstet Gynecol.* 1983;62:180-184.

Conceptus.

Conceptus Incorporated
1021 Howard Avenue
San Carlos, CA 94070 USA

For reorders call: 1-877-ESSURE2, prompt 2 (1-877-377-8732, prompt 2)

CC-0475-01 26.Jul.04F

P6200014 RB C2

PMA REPORT ROUTE SLIP

PMA NUMBER P020014/R008 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.
SHORT NAME CONCEPTUS
CONTACT MS. SUSAN M ALOYAN
DIVISION
ADDRESS 1021 HOWARD AVE.
SAN CARLOS, CA 94070
PHONE NO. (650) 628-4700 FAX NO. (650) 802-2890

MANUFACTURER CONCEPTUS, INC. REG NO. 2951250
STERIGENICS US, INC. 2011171

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

DATE ON SUBMISSION 15-MAR-2005

CYCLE # 1

DATE RECEIVED IN ODE 16-MAR-2005 CURRENT CYCLE 22-APR-2002

DATE FILING DUE

	ELAPSED	LAST CYCLE
FDA TIME	175	175
MFR TIME	21	21

DATE DECISION DUE 14-JUN-2005

REPORT/ AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
Report 001	LOGN	10-FEB-2003	
A001	LOGN	19-FEB-2003	
Report 002	LOGN	31-MAR-2003	11-APR-2003
D001	NORE	11-APR-2003	
Report 003	LOGN	04-AUG-2003	03-NOV-2003
C001	RDEF	03-NOV-2003	25-NOV-2003
Report 004	LOGN	10-NOV-2003	
A001	RDEF	25-NOV-2003	
A001	LOGN	21-JAN-2004	
Report 005	LOGN	29-JAN-2004	
A002	LOGN	04-FEB-2004	10-FEB-2004
C001	RDEF	10-FEB-2004	31-MAR-2004
A001	LOGN	27-FEB-2004	03-MAY-2004
Report 006	LOGN	15-MAR-2004	
A003	RDEF	31-MAR-2004	08-JUN-2004

PMA REPORT ROUTE SLIP

C001	RDEF	03-MAY-2004	18-MAY-2004
A002	RDEF	18-MAY-2004	09-JUN-2004
A001	LOGN	28-MAY-2004	09-JUN-2004
D001	NORE	08-JUN-2004	
D001	NORE	09-JUN-2004	
D001	NORE	09-JUN-2004	
Report 007	LOGN	09-FEB-2005	02-MAR-2005
D001	NORE	02-MAR-2005	

P020014/R8	OGDB
Conceptus, Inc. – Essure™ System for Permanent Birth Control	

Reviewer: Michael T. Bailey, Ph.D.
Biologist

Division/Branch: DRARD/OGDB
(HFZ-470)

Sponsor: Conceptus, Inc.
1021 Howard Ave.
San Carlos, CA 94070

Contact: Edward J. Sinclair
Phone: 650-628-4790
FAX: 650-802-2890

Device Name: Essure™ System

Indication for Use
The Conceptus Essure™ System is indicated for permanent birth control (female sterilization) by bilateral oviduct occlusion.

Device Description
The Essure™ System is composed of three components: 1) Essure™ Micro-insert, 2) Essure™ Delivery System, and 3) Split Introducer.

Purpose of Review
Report 8 was initially submitted as a supplement requesting modifications to device labeling to include results from their postapproval study and to request early termination of their postapproval study based on results to date. In a cover note from Lisa Fisher, she stated that due to the requirement for periodical reports of study results, this submission was logged in as a postapproval report. We have been advised to conduct our review and resolve any deficiencies that we might have following our review. Following addressing any outstanding issues we can identify 1) what labeling changes are needed in light of the study results, and 2) whether the data collected satisfy the condition of approval and can be considered a final report.

Status of Post-Approval Study

Purpose of the Post-Approval Study
The Post-Approval Study was conducted to document the bilateral placement rate for newly trained physicians. The results of these studies will be used to evaluate training procedures and update device labeling. Data collected includes the following:

- Rates of successful bilateral placement of the Essure device at first attempt;
- Identification of factors predictive of failure to achieve bilateral placement of the Essure device at first attempt.

Study Design
This study was designed to collect demographic and micro-insert placement data on a total of 800 women collected by a minimum of 40 physicians in the commercial setting in whom an Essure device is placed through the operating channel of a hysteroscope.

Interim Study Results
As of January 24, 2005, a total o(b)(4)hysicians a(b)(4)US sites have initiated Essure placement procedures as part of the Post-Approval Study. A total o(b)(4)women had been enrolled in this study at that time. Please see the patient tree below.

(b)(4)

In (b)(4) women, the Essure device was not passed through the hysteroscope, primarily due to non-visualization of one-or both fallopian tubes during hysteroscopy. As the study design indicates that only women who have a Essure device placed through the operating channel of the hysteroscope will be included in data analyses, the sponsor has excluded these (b)(4) women. **Based on the study design, this seems appropriate.**

Among the remaining (b)(4) women in whom at least one Essure device was passed through the hysteroscope, bilateral placement was achieved in (b)(4) resulting in an "unadjusted" bilateral placement rate of (b)(4) (b)(4) The lower confidence bound excludes 86%, the placement rate in the pre-approval study, indicating that the placement rate in the Post-Approval Study is currently significantly higher.

(b)(4)

(b)(4)

(b)(4)

Predictors of Placement Rate

(b)(4)

Justification for Early Study Termination

(b)(4)

The target sample size for the Post-Approval Study was 40 physicians and 800 total patients. As of January

(b)(4)

(b)(4)

(b)(4)

Labeling

As mentioned above, in the cover note from Lisa Fisher, we have been advised to conduct our review and resolve any deficiencies that we might have following our review. Following addressing any outstanding issues we can identify 1) what labeling changes are needed in light of the study results, and 2) whether the data collected satisfy the condition of approval and can be considered a final report. Therefore, the sponsor's proposed labeling will not be reviewed until after all of the review-related deficiencies can be addressed.

Consulting Reviews – See attached reviews

Julia Corrado, M.D. – Clinical Review
Nilsa Loyo-Berrios, Ph.D., M.S. – Epidemiology Review
Yihua "Mary" Zhao, Ph.D. – Statistical Review

Review Summary and Conclusions

(b)(4)

(b)(4)

(b)(4)

2.

3.

Recommendation/Conclusion

The review team has indicated that the sponsor has adequately addressed our questions regarding the postapproval study. In addition, the review team finds the data collected from the (b)(4) women enrolled in the study to be sufficient to allow early termination of the postapproval study.

Michael T. Bailey, Ph.D Dated: 8/29/05

Julia Corrado, M.D. Dated: 8/31/05

Colin M. Pollard Date: 8/31/05
Branch Chief, OB/GYN Devices / / Concur
/ / Do not concur

Prepared by: Michael T. Bailey 8/29/05

August 16, 2005

From: Mathematical Statistician Yihua (Mary) Zhao, HFZ-550
Division of Biostatistics, OSB

Subject: Statistical Review of PMA P020014/R08A01 – Interim Report on the Post Approval Study for Newly Trained Physicians and Request for Early Study Termination, Conceptus Essure® System for Permanent Birth Control, Conceptus, Inc. (June 30, 2005)

To: Michael T. Bailey, HFZ-470
Division of Reproductive, Abdominal, and Radiological Devices, ODE

Executive Summary

(b)(4)

Reviewer's Comments

I. (b)(4)

Y. Zhao
8/16/2005

(b)(4)

II.

(b)(4)

III.

Conclusion

(b)(4)

Yihua (Mary) Zhao, Ph.D.

cc:

Nancy Brogdon	HFZ-470
Dave Segerson	HFZ-470
Colin Pollard	HFZ-470
Julia Corrado, M.D.	HFZ-470

Diane Mitchell, M.D.	HFZ-470
Telba Z. Irony, Ph.D.	HFZ-550
Phyllis M. Silverman	HFZ-550
Danica Marinac-Dabic, M.D., Ph.D.	HFZ-541
Nilsa Loyo-Berríos, Ph.D., M.S.	HFZ-541
BIMO	HFZ-310
Medical Device File	
Board File	

Y. Zhao
8/16/2005

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Administration

Public Health Service
Food and Drug

Memorandum

Date: August 3, 2005

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

Subject: Epidemiologic review of the PMA P020014/R8 – Modification of Essure Placement Rate Labeling and Request for Early Termination of the Post Approval Study for Newly Trained Physicians, Conceptus Essure® Permanent Birth Control System, Conceptus, Inc.

To: Michael Bailey, PhD, Lead Reviewer, DRARD, ODE

Through: Danica, Marinac-Dabic, MD, PhD, Chief, EB/DPS/OSB
Thomas Gross, MD, MPH, Director, DPS/OSB

Purpose

The purpose of this memorandum is to provide the epidemiologic review of the Amendment #1 to P020014/R8 Interim Report on the Post-Approval Study for Newly Trained Physicians and Request for Early Study Termination, Conceptus Essure® Permanent Birth Control System, Conceptus, Inc.

Background

(b)(4)

1. (b)(4)
2.
3.

(b)(4)

Conclusions and Recommendations:

The data supports sponsor's claim of better success rate in the post-market setting compared to pre-market.

Nilsa Loyo-Berríos, PhD MS, EB/DPS/OSB

cc: Yihua (Mary) Zhao, HFZ-550
Julia Corrado, MD, HFZ-470

Bailey, Michael T

[redacted]m: Zhao, Yihua
[redacted]t: Wednesday, August 24, 2005 2:26 PM
To: Bailey, Michael T
Cc: Zhao, Yihua
Subject: RE: P020014/R8 Conceptus

Michael,

Thanks for sending the information. My answer to Nilsa's concern doesn't change. The sponsor used (b)(4)

(b)(4)

Yihua Zhao
Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]t: Wednesday, August 24, 2005 2:15 PM
To: Zhao, Yihua
Subject: RE: P020014/R8 Conceptus

Here is the stat justification page from the original post-approval plan in 2002. Let me know if this changes your answer to your previous response.

Please note that I lifted this information from Image, so there are some horrible formatting issues that I could not quickly resolve (including lack of a table).

Essure
tapproval.doc (43 K

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Appendix B

Statistical Analysis Plan

Calculation of Placement Rates and Predictors of Placement Failure
Definition of Outcomes

We define the following outcomes:

Rate of non-attempts: number of women in whom no device is placed through the operating channel of the hysteroscope divided **by** the number in whom hysteroscopy is performed with the intent of bilateral device placement

Bilateral placement rate: number of women who achieve bilateral placement in the first placement procedure divided **by** the number of women in whom hysteroscopy is performed with the intent of bilateral device placement. Bilateral placement rate will **be** calculated as a whole (all physicians together) and **per** physician.

Bilateral placement rate without known confounding patient variables: Bilateral placement rate will also be calculated after excluding women in whom follow-up HSG demonstrates either PTO or unicornuate uterus. Exclusion of such women is appropriate since bilateral placement in these women is, by definition, impossible.

Predictors of Placement Rates

The first set of analyses will determine if there ***are*** any demographic, clinical or procedure-related variables that predict successful bilateral device placement (see section 4 of the protocol). To increase sample size, data from the pre-approval clinical trials (Phase 11 and Pivotal trials: IDES **#G980152** and *#G000055,* respectively) will be pooled with that collected in the commercial setting. We will report data in tabular format. We will then use logistic regression to determine the odds of bilateral placement by variouscharacteristics. Further models will be examined which treat physician as a randomiexchangeable effect. These analyses will use the SAS macro "GLIMMIX" to performed mixed (random and fixed effects) logistic regression.

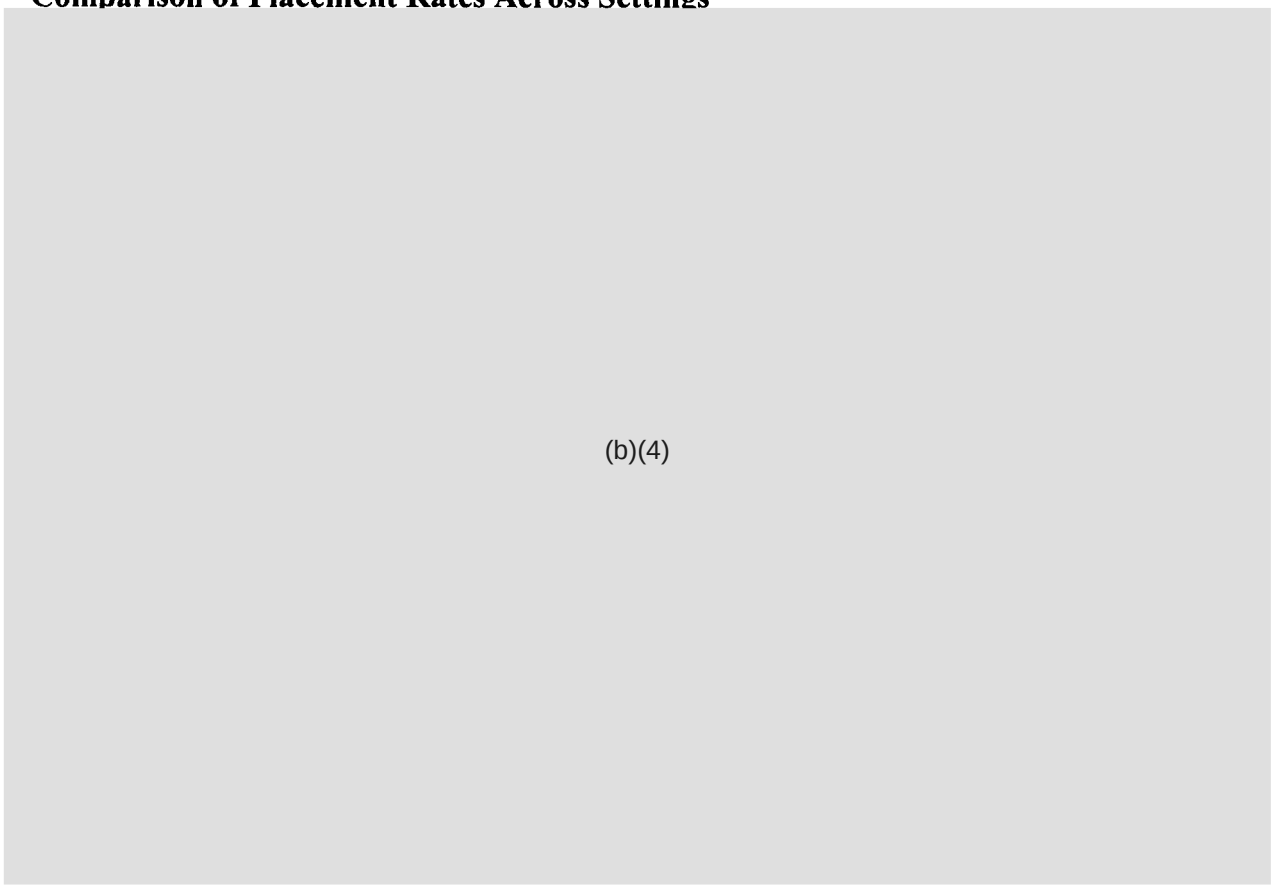
Overall Placement Rate

Using the data from the commercial setting, we will determine the bilateral placement rate with 95% confidence limits. Both fixed effects and random effects estimates (treating physician as a random effect) will be examined

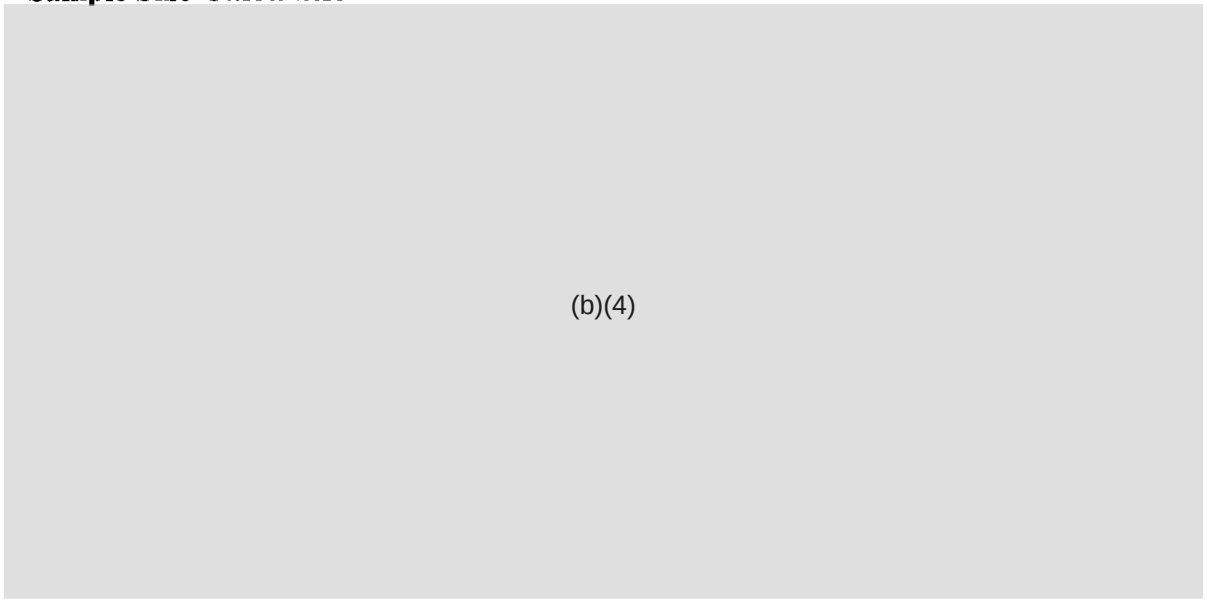
Target Placement Rate for Comparison

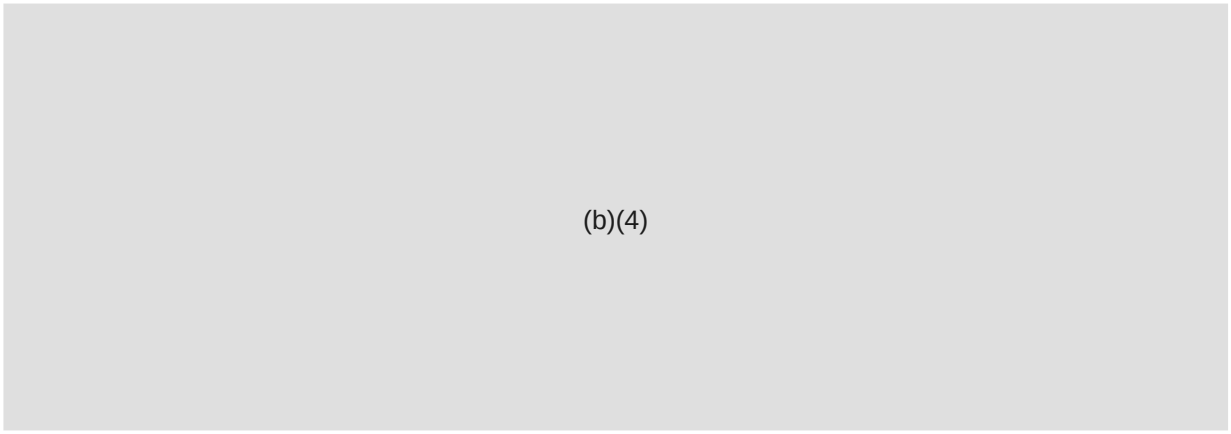
Among women in the Pivotal trial (b)(4) achieved bilateral placement during the first procedure. This same placement rate will be used as the target for the post-approval study.

Comparison of Placement Rates Across Settings



Sample Size Calculation




(b)(4)

Bailey, Michael T

[redacted]m: Loyo-Berrios, Nilsa
[redacted]t: Wednesday, August 24, 2005 1:46 PM
To: Zhao, Yihua; Bailey, Michael T
Subject: RE: P020014/R8 Conceptus

Thanks Mary.

-----Original Message-----
From: Zhao, Yihua
Sent: Wednesday, August 24, 2005 1:43 PM
To: Bailey, Michael T; Loyo-Berrios, Nilsa
Cc: Zhao, Yihua
Subject: RE: P020014/R8 Conceptus

Nilsa and Michael,

(b)(4)

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]t: Wednesday, August 24, 2005 1:31 PM
To: Zhao, Yihua
Subject: FW: P020014/R8 Conceptus

Mary,

Please respond to Nilsa's comments below. Thanks.

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Loyo-Berrios, Nilsa
Sent: Wednesday, August 24, 2005 1:26 PM
To: Bailey, Michael T
Cc: Marinac-Dabic, Danica
Subject: RE: P020014/R8 Conceptus

Hello Michael,

(b)(4)

I am working at home today, if you have any questions you can contact me via e-mail or you can call 410-581-0860.

-Nilsa

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]t: Wednesday, August 24, 2005 1:03 PM
To: Loyo-Berrios, Nilsa
Subject: P020014/R8 Conceptus

Nilsa,

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

[redacted]m: Mitchell, Diane A.
[redacted]t: Wednesday, August 17, 2005 6:52 PM
To: Bailey, Michael T; Pollard, Colin M.; Zhao, Yihua
Cc: Corrado, Julia A; Marinac-Dabic, Danica; Loyo-Berrios, Nilsa
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Diane
301 594 5072 x123

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]t: Wednesday, August 17, 2005 1:47 PM
To: Pollard, Colin M.; Mitchell, Diane A.; Zhao, Yihua
Cc: Corrado, Julia A; Marinac-Dabic, Danica; Loyo-Berrios, Nilsa
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

[redacted]n: Pollard, Colin M.
[redacted]t: Wednesday, August 17, 2005 1:28 PM
To: Zhao, Yihua; Mitchell, Diane A.; Bailey, Michael T
Cc: Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Colin

Bailey, Michael T

[redacted]m: Zhao, Yihua
[redacted]t: Wednesday, August 17, 2005 12:23 PM
To: Pollard, Colin M.; Mitchell, Diane A.; Bailey, Michael T
Cc: Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- *Conceptus* Post-Approval Study for Newly Trained Physicians

(b)(4)

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]m: Pollard, Colin M.
[redacted]t: Wednesday, August 17, 2005 12:18 PM
To: Mitchell, Diane A.; Zhao, Yihua; Bailey, Michael T
Cc: Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Colin

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]nt: Wednesday, August 17, 2005 11:44 AM
To: Mitchell, Diane A.; Zhao, Yihua
Cc: Pollard, Colin M.; Corrado, Julia A; Marinac-Dabic, Danica; Loyo-Berrios, Nilsa
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

P020014-R8 Essure Rev Final.do...

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

[redacted]m: Mitchell, Diane A.
[redacted]t: Wednesday, August 17, 2005 11:39 AM
To: Bailey, Michael T
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

Sounds good

Diane
301 594 5072 x123

-----Original Message-----
From: Bailey, Michael T
Sent: Wednesday, August 17, 2005 11:35 AM
To: Mitchell, Diane A.; Zhao, Yihua
Cc: Pollard, Colin M.; Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

From: Mitchell, Diane A.
Sent: Wednesday, August 17, 2005 11:32 AM
To: Zhao, Yihua; Bailey, Michael T
Cc: Pollard, Colin M.; Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Diane
301 594 5072 x123

-----Original Message-----
From: Zhao, Yihua
Sent: Wednesday, August 17, 2005 11:28 AM
To: Mitchell, Diane A.; Bailey, Michael T
Cc: Pollard, Colin M.; Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

Diane,

(b)(4)

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]m: Mitchell, Diane A.
[redacted]t: Wednesday, August 17, 2005 11:11 AM
To: Zhao, Yihua; Bailey, Michael T
Cc: Pollard, Colin M.; Corrado, Julia A; Marinac-Dabic, Danica
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Diane
301 594 5072 x123

-----Original Message-----
From: Zhao, Yihua
Sent: Tuesday, August 16, 2005 9:58 AM
To: Bailey, Michael T
Cc: Brogdon, Nancy C.; Segerson, Dave; Pollard, Colin M.; Corrado, Julia A; Mitchell, Diane A.; Irony, Telba Z.; Silverman, Phyllis M.; Marinac-Dabic, Danica; Loyo-Berrios, Nilsa; Bobbitt, Margaret; Zhao, Yihua
Subject: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

Michael,

(b)(4)

<< File: P020014r8a1.doc >>

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]: Zhao, Yihua
[redacted]: Tuesday, August 16, 2005 11:38 AM
To: Bailey, Michael T
Cc: Zhao, Yihua
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

[redacted]m: Bailey, Michael T
[redacted]t: Tuesday, August 16, 2005 10:54 AM
To: Zhao, Yihua
Subject: RE: Statistical Review of PMA P020014/R08A01 -- Conceptus Post-Approval Study for Newly Trained Physicians

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

P020014/R8	OGDB
Conceptus, Inc. – Essure™ System for Permanent Birth Control	

Reviewer:	Michael T. Bailey, Ph.D. Biologist	**Division/Branch:**	DRARD/OGDB (HFZ-470)

Sponsor:	Conceptus, Inc. 1021 Howard Ave. San Carlos, CA 94070	**Contact:**	Edward J. Sinclair Phone: 650-628-4790 FAX: 650-802-2890

Device Name: Essure™ System

Indication for Use
The Conceptus Essure™ System is indicated for permanent birth control (female sterilization) by bilateral oviduct occlusion.

Device Description
The Essure™ System is composed of three components: 1) Essure™ Micro-insert, 2) Essure™ Delivery System, and 3) Split Introducer.

Purpose of Review
Report 8 was initially submitted as a supplement requesting modifications to device labeling to include results from their postapproval study and to request early termination of their postapproval study based on results to date. In a cover note from Lisa Fisher, she stated that due to the requirement for periodical reports of study results, this submission was logged in as a postapproval report. We have been advised to conduct our review and resolve any deficiencies that we might have following our review. Following addressing any outstanding issues we can identify 1) what labeling changes are needed in light of the study results, and 2) whether the data collected satisfy the condition of approval and can be considered a final report.

Status of Post-Approval Study

Purpose of the Post-Approval Study
The Post-Approval Study was conducted to document the bilateral placement rate for newly trained physicians. The results of these studies will be used to evaluate training procedures and update device labeling. Data collected includes the following:

- Rates of successful bilateral placement of the Essure device at first attempt;
- Identification of factors predictive of failure to achieve bilateral placement of the Essure device at first attempt.

Study Design
This study was designed to collect demographic and micro-insert placement data on a total of 800 women collected by a minimum of 40 physicians in the commercial setting in whom an Essure device is placed through the operating channel of a hysteroscope.

Interim Study Results
As of January 24, 2005, a total of (b)(4) physicians at (b)(4) S sites have initiated Essure placement procedures as part of the Post-Approval Study. A total of (b)(4) women had been enrolled in this study at that time. Please see the patient tree below.

(b)(4)

(b)(4)

(b)(4)

(b)(4)

Recommendation
Request additional information.

Michael T. Bailey, Ph.D Dated: 6/9/05

Julia Corrado, M.D. Dated: 6/9/05

Colin M. Pollard Date: /✓/ Concur
Branch Chief, OB/GYN Devices / / Do not concur

Prepared by: Michael T. Bailey 6/7/05

Bailey, Michael T

From: Corrado, Julia A
Sent: Tuesday, June 07, 2005 1:42 PM
To: Bailey, Michael T
Cc: Zhao, Yihua; Loyo-Berrios, Nilsa; Pollard, Colin M.
Subject: Clinical review of P020014/R8 re Essure post-approval bilateral placement rate

June 7, 2005

Mike,

(b)(4)

Thanks!

Julia

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Administration

Public Health Service
Food and Drug

Memorandum

Date: May 9, 2005

From Nilsa Loyo-Berríos, PhD MS. Epidemiology Branch, DPS/OSB, HFZ-541, Division of Postmarket Surveillance (DPS), Office of Surveillance and Biometrics (OSB)

Subject: Epidemiologic review of the PMA P020014/R8 – Modification of Essure Placement Rate Labeling and Request for Early Termination of the Post Approval Study for Newly Trained Physicians, Conceptus Essure® Permanent Birth Control System, Conceptus, Inc.

To: Michael Bailey, PhD, Lead Reviewer, DRARD, ODE

Through: Danica, Marinac-Dabic, MD, PhD, Chief, EB/DPS/OSB
Thomas Gross, M.D., M.P.H., Director, DPS/OSB

Purpose

The purpose of this memorandum is to provide the epidemiologic review of the PMAP020014/R8 Modification of Essure Placement Rate Labeling and Request for Early Termination of the Post Approval Study for Newly Trained Physicians, Conceptus Essure® Permanent Birth Control System, Conceptus, Inc.

Background

This PMA supplement contains results from the "Post Approval Study for Newly Trained Physicians", as well as a petition for early termination of the study and it also proposes changes for labeling based on the new data available from this study.

The objectives of the study were:

1. To determine the rates for successful bilateral placement of Essure System at first attempt.
2. To identify factors predictive of failure to achieve bilateral placement of the Essure System at first attempt.
3. (b)(4)

Bilateral Placement Success Rates

(b)(4)

Analysis on Predictive Factors

(b)(4)

(b)(4)

Comparison Placement Success Rates: Commercial Setting vs. Clinical Setting

(b)(4)

(b)(4)

Conclusions and Recommendations:

(b)(4)

Nilsa Loyo-Berríos, PhD MS, EB/DPS/OSB

cc: Yihua (Mary) Zhao, HFZ-550
Julia Corrado, MD, HFZ-470

May 3, 2005

From: Mathematical Statistician Yihua (Mary) Zhao, HFZ-550
Division of Biostatistics, OSB

Subject: Statistical Review of PMA P020014/R8 – Modification of Essure Placement Rate Labeling and Request for Early Termination of the Post Approval Study for Newly Trained Physicians, Conceptus Essure® Permanent Birth Control System, Conceptus, Inc. (March 15, 2005)

To: Michael T. Bailey, HFZ-470
Division of Reproductive, Abdominal, and Radiological Devices, ODE

Executive Summary

In this PMA supplement, the sponsor reported data and analysis results from the post-approval study for newly trained physicians. The sponsor proposed to terminate this post-approval study and to add the findings from this study to the physician and patient labelings.

Pre-Market Approval (P020014) to the Conceptus Essure® Permanent Birth Control System was granted by FDA on November 4, 2002, and Conceptus agreed to provide data on a post-approval study in the U.S. with newly trained physicians in post approval reports. This post-approval study was originally designed to collect demographic and micro-insert placement data on a total of 800 women from 40 physicians in the commercial setting in whom an Essure System is placed through the operating channel of the hysteroscope. Data collected will include: (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. As of January 24, 2005 (the date of the last data extract), a total of (b)(4) physicians at (b)(4) U.S. sites have initiated Essure placement procedures as part of this post-approval study. A total of (b)(4) women have been enrolled and micro-insert placement was attempted in 494 women. Among these (b)(4) women were considered to have uterine anatomy that, by definition, prevented bilateral placement and were excluded from the adjusted placement rate, therefore reducing the total number of women to (b)(4)

(b)(4)

(b)(4)

Reviewer's Comments

(b)(4)

this Supplement that I do not include here.) The other one is 91.2% (446/489) as

(b)(4)

Conclusion

(b)(4)

Yihua (Mary) Zhao, Ph.D.

cc:

Nancy Brogdon	HFZ-470
Dave Segerson	HFZ-470
Colin Pollard	HFZ-470
Julia Corrado, M.D.	HFZ-470
Diane Mitchell, M.D.	HFZ-470
Telba Z. Irony, Ph.D.	HFZ-550
Danica Marinac-Dabic, Ph.D.	HFZ-550
BIMO	HFZ-310
Medical Device File	
Board File	

Bailey, Michael T

[redacted]om: Zhao, Yihua
[redacted]ent: Thursday, June 09, 2005 9:16 AM
To: Bailey, Michael T; Loyo-Berrios, Nilsa; Corrado, Julia A; Pollard, Colin M.
Cc: Zhao, Yihua
Subject: RE: P020014/R8 Conceptus Post-Approval Report

(b)(4)

Yihua Zhao
Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

Bailey, Michael T

From: Bailey, Michael T
Sent: Thursday, June 09, 2005 8:33 AM
To: Loyo-Berrios, Nilsa; Zhao, Yihua; Corrado, Julia A; Pollard, Colin M.
Subject: P020014/R8 Conceptus Post-Approval Report

Hello All,

(b)(4)

P020014-R8
SURE.AI.MTB.6-7-0

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

From: Corrado, Julia A
Sent: Wednesday, June 08, 2005 11:17 AM
To: Loyo-Berrios, Nilsa; Bailey, Michael T; Pollard, Colin M.
Cc: Zhao, Yihua; Fisher, Lisa C.; Marinac-Dabic, Danica
Subject: RE: Conceptus Postapproval Report

Mike et al,

(b)(4)

Thanks,

Julia

-----Original Message-----
From: Loyo-Berrios, Nilsa
Sent: Tuesday, June 07, 2005 5:20 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Zhao, Yihua; Fisher, Lisa C.; Marinac-Dabic, Danica
Subject: RE: Conceptus Postapproval Report

Hello Michael,

(b)(4)

-Nilsa

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:41 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Might help if I actually attach the files I am looking to receive comments on!!!!

<< File: P020014-R8 Essure Rev 6-05.doc >> << File: P020014-R8 ESSURE.AI.MTB.6-7-05.DOC >>

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB

(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:30 PM
To: Pollard, Colin M.
Cc: *Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.*
Subject: Conceptus Postapproval Report

Colin,

Please look over and comment on my review and letter for the PMA report from Conceptus regarding their Postapproval Study. Please note that I am not sure that I used the correct letter template (Lisa please let me know if this is acceptable). Please note that this file has a branch due date of June 9. Thanks.

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

From: Bailey, Michael T
Sent: Wednesday, June 08, 2005 7:51 AM
To: Pollard, Colin M.; Corrado, Julia A
Subject: FW: Conceptus Postapproval Report

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Loyo-Berrios, Nilsa
Sent: Tuesday, June 07, 2005 5:20 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Zhao, Yihua; Fisher, Lisa C.; Marinac-Dabic, Danica
Subject: RE: Conceptus Postapproval Report

Hello Michael,

Very good job with the review!

(b)(4)

-Nilsa

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:41 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Might help if I actually attach the files I am looking to receive comments on!!!!

<< File: P020014-R8 Essure Rev 6-05.doc >> << File: P020014-R8 ESSURE.AI.MTB.6-7-05.DOC >>

Michael T. Bailey, Ph.D.

FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:30 PM
To: Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: Conceptus Postapproval Report

Colin,

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Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by email or telephone.

Bailey, Michael T

From: Bailey, Michael T
Sent: Wednesday, June 08, 2005 7:32 AM
To: Zhao, Yihua
Subject: RE: Conceptus Postapproval Report

Mary,

(b)(4)

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Zhao, Yihua
Sent: Tuesday, June 07, 2005 5:36 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Michael,

(b)(4)

Yihua Zhao

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:41 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Might help if I actually attach the files I am looking to receive comments on!!!!

<< File: P020014-R8 Essure Rev 6-05.doc >> << File: P020014-R8 ESSURE.AI.MTB.6-7-05.DOC >>

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----

From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:30 PM
To: Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: Conceptus Postapproval Report

Colin,

Please look over and comment on my review and letter for the PMA report from Conceptus regarding their Postapproval Study. Please note that I am not sure that I used the correct letter template (Lisa please let me know if this is acceptable). Please note that this file has a branch due date of June 9. Thanks.

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

From: Zhao, Yihua
Sent: Tuesday, June 07, 2005 5:36 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Michael,

(b)(4)

Yihua (Mary) Zhao, Ph.D.
FDA/CDRH/OSB/DBS/GSDB
Office 120C, 1350 Piccard Drive, HFZ-550
Rockville, Maryland 20850
Phone: 301-827-9721 Fax: 301-443-8559
E-Mail: yxz@cdrh.fda.gov

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:41 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

Might help if I actually attach the files I am looking to receive comments on!!!!

<< File: P020014-R8 Essure Rev 6-05.doc >> << File: P020014-R8 ESSURE.AI.MTB.6-7-05.DOC >>

Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:30 PM
To: Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: Conceptus Postapproval Report

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FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

Bailey, Michael T

From: Loyo-Berrios, Nilsa
Sent: Tuesday, June 07, 2005 5:20 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Zhao, Yihua; Fisher, Lisa C.; Marinac-Dabic, Danica
Subject: RE: Conceptus Postapproval Report

Hello Michael,

Very good job with the review!

(b)(4)

-Nilsa

-----Original Message-----
From: Bailey, Michael T
Sent: Tuesday, June 07, 2005 4:41 PM
To: Bailey, Michael T; Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: RE: Conceptus Postapproval Report

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FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

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Sent: Tuesday, June 07, 2005 4:30 PM
To: Pollard, Colin M.
Cc: Corrado, Julia A; Loyo-Berrios, Nilsa; Zhao, Yihua; Fisher, Lisa C.
Subject: Conceptus Postapproval Report

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Michael T. Bailey, Ph.D.
FDA/CDRH/OGDB
(301)594-1180
michael.bailey@fda.hhs.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food And Drug Administration

Memorandum

Date: March 22, 2005

From: Lisa Fisher, PMA Section/Program Operations Staff/ODE Lisa Fisher

Subject: Conceptus, Inc.
P020014/R8 – Essure System

To: File

On 3/16/05, Conceptus, Inc submitted a PMA supplement in order to modify the Essure device labeling to include results from their postapproval study and to request early termination of the postapproval study based on the results. The submission contains the final study report. **Since the applicant is required to provide periodic reports on the study results, the submission has been logged in as a postapproval report.** Once CDRH has had an opportunity to review the report and resolve any deficiencies then we can ideintify 1) what labeling changes are needed in light of the study results, and 2) whether the data collected satisfy the condition of approval and can be considered a final report.

If the data can be considered a final report, please use boilerplate letter at H: PMA/Reports/ Postapproval/Postapproval Study Completed. The letter includes an optional paragraph for CDRH to identify any necessary labeling changes and instructs the applicant to submit the information via a supplement.

The applicant was contacted by telephone on 3/18/05 and advised of the above decision.

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

March 18, 2005

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

Dear Sirs:

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

PMA Number: P020014/R008
Dated: 15-MAR-2005
Received: 16-MAR-2005
Device: ESSURE SYSTEM

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

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

Sincerely yours,

Karen Oliver
Program Manager
Division of Reproductive, Abdominal,
and Radiological Devices

Office of Device Evaluation
Center for Devices and
Radiological Health

P020014/R8/C2

Conceptus®

March 15, 2005

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

2005 MAR 16 A 10:35

RE: **PMA supplement for modification of Essure placement rate labeling and request for early termination of the Post Approval Study for Newly Trained Physicians**

P020014, Conceptus Essure® System for Permanent Birth Control

To Whom it May Concern,

In accordance with 21 CFR 814.39(a), Conceptus is submitting the enclosed PMA supplement for modification of the Essure placement rate labeling and request early termination of the Post Approval Study for Newly Trained Physicians.

Background

The Food and Drug Administration granted Pre-Market Approval (P020014) to the Conceptus Essure System on November 4, 2002. In the approval letter, Conceptus agreed to provide data on a post approval study in the U.S. with newly trained physicians in post approval reports. This study was intended to document the bilateral placement rate for newly trained physicians (800 patients, 40 physicians, first 20 attempts). These data were intended to evaluate the training procedures and to update labeling. Data collection included 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.

Interim Study Results - Essure Placement Rate

As of January 24, 2005 (the date of the last data extract), a total of (b)(4) hysicians a (b)(4) JS sites have initiated Essure placement procedures as part of the Post Approval Study. A total o (b)(4) omen have been enrolled and a complete clinical data report is presented in ***Exhibit 1*** of this supplement. The report summarizes physician, patient and procedure data. A variety of placement rates have been calculated in Section "J" of the clinical data report based on excluding confounding factors or analyzing differences between device designs.

Conceptus proposes to modify our physician and patient labeling with data from the Post Approval Study for Newly Trained Physicians based on a detailed statistical analysis performed by Daniel Cher, MD. This placement rate summary is provided in ***Exhibit 2*** of this supplement.

As the summary report indicates, (b)(4) omen were enrolled into the Post Approval Study. In (b)(4) omen, the Essure device was not passed through the hysteroscope, primarily due to non-visualization of one or both fallopian tubes on hysteroscopy. Since device placement cannot be attempted if tubes are not visualized hysteroscopically, all device placement analyses excluded these "non-attempts."

Among the (b)(4) women in whom at least one Essure device was passed through the hysteroscope, bilateral placement was achieved in (b)(4) resulting in an "unadjusted" bilateral placement rate of (b)(4) The lower confidence bound excludes (b)(4) the placement rate in the pre-approval study, which indicates that the placement rate in the post-approval setting is statistically significantly higher.

(b)(4)

Despite device placement attempts, in (b)(4) women no device was placed in either tube.

Adjusted Bilateral Placement Rate

(b)(4)

(b)(4)

Predictors of Placement Rate

(b)(4)

Justification for Early Study Termination

In the post-approval study protocol, the target sample size was 40 physicians with 800 total patients. To date, (b)(4) physicians have enrolled (b)(4) women, leaving (b)(4) women remaining to achieve the study's stated target sample size. As shown above, analysis of current data strongly supports the argument that placement rate in the post-approval study is better than in the pre-approval pivotal trial. We argue here that further recruitment and study of placement rates in the post-approval setting is not necessary.

Consistent with Conceptus' previous use of Bayesian models, we used a Bayesian predictive model[1] to estimate the distribution of the total expected number of failures if 286 more women[2] (which would bring the total to 800) were to be subsequently enrolled and treated. The "current" failure rate is 19/477 or 4.0%; thus, if 286 more women were recruited and treated, we would expect, on average, 11.5 more failures.[3] However, given random variation, we might expect fewer or more failures than 11.5. The predictive distribution takes into account this added variation.

(b)(4)

(b)(4)

Labeling Changes

Based on the modified placement rate data presented in ***Exhibit 2*** of this supplement, Conceptus proposes to integrate the new data into the physician labeling (Instructions for Use) and the patient labeling (Patient Information Booklet).

A. Physician Labeling

The proposed changes in the *Essure Instructions For Use* are provided in ***Exhibit 3*** of this supplement. The old text is displayed as ~~strikethrough~~ with the newer, or replacement text displayed with underlines.

(b)(4)

B. Patient Labeling

The proposed changes in the *Essure Patient Information Booklet* are provided in ***Exhibit 4*** of this supplement. The old text is displayed as ~~strikethrough~~ with the newer, or replacement text displayed with underlines.

(b)(4)

Exhibits

1. Clinical Data Report: Post Approval Study for Newly Trained Physicians
2. Placement Rate Summary: Post Approval Study for Newly Trained Physicians
3. Physician Labeling Changes
   The *Essure Instructions for Use* showing text modifications related to the Post Approval Study and Essure placement rates.
4. Patient Labeling Changes
   The *Essure Patient Information Booklet* showing text modifications related to the Post Approval Study and Essure placement rates.

The information contained in this PMA supplement is considered confidential and Conceptus therefore requests protection of this information in accordance with 18 USC 1905, 21 USC 331(I), 5 USC 552.

Please let me know if you have any questions or need additional information. I can be reached by phone at (650) 628-4790, by fax at (650) 802-2890, or by email at esinclair@conceptus.com.

Sincerely,

Edward J. Sinclair
Vice President, Clinical Research, Regulatory Affairs and Quality Assurance
Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070 USA
(650) 628-4700

Exhibits: 1-4

P0200I4 R8 A1 C1

P020014/R8/A1 C1

Conceptus.

June 30, 2005

Dr. Michael Bailey
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 P020014/R8**

Interim Report on the Post Approval Study for Newly Trained Physicians and Request for Early Study Termination

P020014, Conceptus Essure® System for Permanent Birth Control

Dear Dr. Bailey,

(b)(4)

1. (b)(4)

(b)(4)

2. (b)(4)

Table 1. Excluded Post Approval Study sites

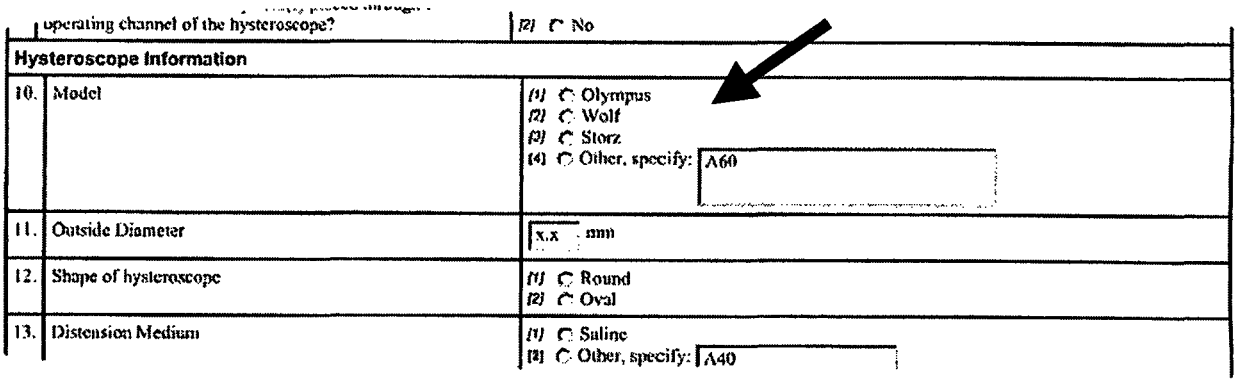
SITE #	LOCATION	INVESTIGATOR	REASON FOR EXCLUSION
(b)(4), (b)(6)			

3. (b)(4)

Table 2. Placement rate by hysteroscope and micro-insert characteristics.

	Bilateral placement
	(b)(4)
(b)(4)	

B. On the study Case Report Forms (recall that we use an electronic case report form system for the Post Approval Study) we ask each investigator to list the type of hysteroscope they used for each placement procedure. As shown in ***Figure 1*** below, we only list three scope manufacturers (Olympus, Wolf and Storz) and allow physicians to specify "Other" by typing in the name of the particular scope utilized.



operating channel of the hysteroscope?		[2] ○ No
Hysteroscope Information		
10.	Model	[1] ○ Olympus [2] ○ Wolf [3] ○ Storz [4] ○ Other, specify: A60
11.	Outside Diameter	X.X mm
12.	Shape of hysteroscope	[1] ○ Round [2] ○ Oval
13.	Distension Medium	[1] ○ Saline [3] ○ Other, specify: A40

Figure 1. Study Case Report Form showing hysteroscope information fields

(b)(4)

(b)(4)

(b)(4)

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Conceptus, Inc.
1021 Howard Avenue
San Carlos, CA 94070 USA
(650) 628-4700

P020014 R8 A1 C2

LDC.

PMA REPORT ROUTE SLIP

PMA NUMBER P020014/R008/A001 PANEL OB DIVISION DRARD BRANCH OGDB

TRADE NAME ESSURE SYSTEM

GENERIC NAME DEVICE, OCCLUSION, TUBAL, CONTRACEPTIVE

PRODUCT CODE HHS INSERT, TUBAL OCCLUSION

APPLICANT CONCEPTUS, INC.
SHORT NAME CONCEPTUS
CONTACT MS. SUSAN M ALOYAN
DIVISION
ADDRESS 1021 HOWARD AVE.
SAN CARLOS, CA 94070
PHONE NO. (650) 628-4700 FAX NO. (650) 802-2890

MANUFACTURER CONCEPTUS, INC. REG NO. 2951250
STERIGENICS US, INC. 2011171

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

DATE ON SUBMISSION 30-JUN-2005

CYCLE # 1

DATE RECEIVED IN ODE 05-JUL-2005 CURRENT CYCLE 22-APR-2002

DATE FILING DUE

	ELAPSED	LAST CYCLE
FDA TIME	175	175
MFR TIME	21	21

DATE DECISION DUE 03-OCT-2005

REPORT/ AMENDMENT/ CORRESPONDENCE	REASON	START	STOP
Report 001	LOGN	10-FEB-2003	
A001	LOGN	19-FEB-2003	
Report 002	LOGN	31-MAR-2003	11-APR-2003
D001	NORE	11-APR-2003	
Report 003	LOGN	04-AUG-2003	03-NOV-2003
C001	RDEF	03-NOV-2003	25-NOV-2003
Report 004	LOGN	10-NOV-2003	
A001	RDEF	25-NOV-2003	
A001	LOGN	21-JAN-2004	
Report 005	LOGN	29-JAN-2004	
A002	LOGN	04-FEB-2004	10-FEB-2004
C001	RDEF	10-FEB-2004	31-MAR-2004
A001	LOGN	27-FEB-2004	03-MAY-2004
Report 006	LOGN	15-MAR-2004	
A003	RDEF	31-MAR-2004	08-JUN-2004

Not a standalone

PMA REPORT ROUTE SLIP

C001	RDEF	03-MAY-2004	18-MAY-2004
A002	RDEF	18-MAY-2004	09-JUN-2004
A001	LOGN	28-MAY-2004	09-JUN-2004
D001	NORE	08-JUN-2004	
D001	NORE	09-JUN-2004	
D001	NORE	09-JUN-2004	
Report 007	LOGN	09-FEB-2005	02-MAR-2005
D001	NORE	02-MAR-2005	
Report 009	LOGN	22-APR-2005	

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

July 06, 2005

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

Dear Sirs:

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

PMA Number: P020014/R008/A001
Dated: 30-JUN-2005
Received: 05-JUL-2005
Device: ESSURE SYSTEM

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

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Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

Sincerely yours,

Karen Oliver
Program Manager
Division of Reproductive, Abdominal,
and Radiological Devices

Office of Device Evaluation
Center for Devices and
Radiological Health

Conceptus®

June 30, 2005

Dr. Michael Bailey
Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
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Rockville, MD 20850

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P020014, Conceptus Essure® System for Permanent Birth Control

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(b)(4)

(b)(4)

2. (b)(4)

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(b)(4)

(b)(4)

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