P020014/R24 C1

Conceptus Inc.

Makers of Essure

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June 11, 2009

FDA CDRH DMC

JUN 16 2009

Received

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

RE: **ESS305 Post-Approval Study: Final report**
PMA P020014, Report #24
Essure® System for Permanent Birth Control ESS305

To Whom It May Concern:

In accordance with 21 CFR 822, Conceptus is submitting three copies of the final report on the ESS305 Post-Approval Study.

The information contained in this final report on the ESS305 Post-Approval Study 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) 962-4078, by fax at (650) 962-5194, or by email at rachelle_acuna-narvaez@conceptus.com.

Sincerely,

Rachelle Ann Narvaez

Rachelle Acuña-Narvaez
Senior Regulatory Affairs Associate

Conceptus

CLINICAL DATA FINAL REPORT: ESS305 POST-APPROVAL STUDY

Data current to May 31, 2009

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A. Post-Approval Study Required Information

Sponsor Information

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Product Information

Product Name: Essure Permanent Birth Control System
Model Number: ESS305
Application Number: P020014 – S012
Date of PMA approval: June 15, 2007

Submission Information

Date of Submission: June 11, 2009
Data included in this submission: Clinical Study Data
Type of Submission: FINAL Post-Approval Study Report
Post-Approval Study Status: Complete

Study Information

The study information follows in the remainder of this report.

B. Background

This report contains data obtained from the U.S. Post-Approval Study for Placement of the ESS305 Essure® System as part of the post-approval requirements for the Essure PMA P020014, Supplement 12 (approval granted by FDA on June 15, 2007).

The data in this report are current to May 31, 2009.

C. Study Purpose and Protocol

Purpose

According to the post-approval requirements, this study is intended to document the bilateral placement rate for the ESS305. These data will be used to evaluate

the training procedures and to update labeling. Data collected include the following:

a. bilateral placement of the ESS305 micro-insert at first attempt;
b. identification of factors predictive of failure to achieve bilateral placement of the ESS305 at first attempt;
c. comparison of bilateral placement success between newly trained physicians and experienced physicians;[1]
d. evaluation of aspects of the ESS305 design that may impact bilateral placement rate;
e. hysteroscopy time to perform the procedure;
f. adverse device effects; and
g. adverse procedure events.

Study Design

This study was designed to collect demographic and micro-insert placement data on a minimum of 800 women from 80 physicians in the commercial setting in whom an ESS305 is placed through the operating channel of the hysteroscope. Data was also collected on subjects in whom the procedure was begun, but in whom an Essure System was not placed through the operating channel of the hysteroscope ("non-attempts"), but this was in addition to the subjects in whom there was an attempt at placement with Essure.

Although only 80 physicians were needed to reach a total of 800 subjects, it was anticipated that up to (b)(4) physicians would be enrolled in this study in the event that not all physicians completed a total of (b)(4) cases, or were unable to do so on a timely basis. Enrollment in this study was planned to cease after data was available from 80 physicians who provided data regarding (b)(4) cases of Essure placement attempts.

Investigator enrollment in this study was limited to no more than (b)(4) physicians from any one state and no more than (b)(4) experienced physicians and/or (b)(4) newly trained physicians from any (b)(4) institution. In addition, no more than (b)(4) of the physicians were to represent (b)(4) (b)(4)

Physicians were enrolled in the study only if: 1) they agreed to participate, and 2) (b)(4)

[1] The study was amended by P020014/S018 to exclude analysis of bilateral placement rate equivalence between experienced and newly trained physicians. See section B, "Study Design" for more information.

site was evaluated to ensure it had an adequate patient base and could provide sufficient staff and documentation support to conduct the study properly.

(b)(4)

The study was initially designed to compare placement data in newly trained physicians with physicians experienced in Essure micro-insert placement (i.e., experienced using the previous ESS205 device). Forty experienced physicians and(b)(4)newly trained physicians were to perform(b)(4)ases each. However,

(b)(4)

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 study endpoints were as follows:

1. Bilateral micro-insert placement rate at first attempt;
2. Comparison of bilateral placement success between newly trained physicians and experienced physicians;[2]
3. Identification of factors predictive of micro-insert placement failure;
4. Evaluation of aspects of the ESS305 design that may impact bilateral placement rate;
5. Hysteroscopy time to perform the procedure;
6. Adverse device effects; and
7. Adverse procedure events.

[2] The study was amended by P020014/S018 to exclude analysis of bilateral placement rate equivalence between experienced and newly trained physicians. See section B, "Study Design" for more information.

The nature and frequency of adverse device effects or adverse procedural events that may occur during or after placement procedure up to discharge was assessed.

(b)(4)

The following demographic information was 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 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, certain procedure details ((b)(4) etc.) were recorded.

Placement Device

The ESS305 System was approved by the Food and Drug Administration under PMA P020014/S12.

Placement Procedure

Micro-insert placement was performed according to the Instructions for Use (IFU) approved under PMA P020014/S12.

Follow-up Procedures

No patient follow-up was conducted as part of this study.

Study Dates

(b)(4)

D. 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 were willing to allow their data to be shared with the Sponsor and the FDA.

E. Study Site Information

A total of (b)(4) physicians at (b)(4) U.S. sites initiated Essure placement procedures as part of the ESS305 Post-Approval Study. A total of 584 subjects were enrolled in the study as shown in ***Table 1***.

Table 1. Number of Subjects Enrolled per Investigator

Location	Investigator	Site	No. of Subjects
Indiana	(b)(6)	1	(b)(4)
California		2	
Missouri		3	
Arizona		4	
Georgia		6	
New York		7	
Florida		8	

Location	Investigator	Site	No. of Subjects
Texas	(b)(6)	9	(b)(4)
Florida		10	
Virginia		11	
Minnesota		12	
Texas		13	
Tennessee		14	
Indiana		15	
New Mexico		16	
Wisconsin		18	
Wisconsin		19	
Wisconsin		20	
Colorado		23	
Massachusetts		24	
Arizona		25	
North Carolina		26	
Kentucky		27	
Ohio		28	
Kentucky		29	
Indiana		30	
Tennessee		31	
Tennessee		32	
New York		33	
New York		34	
California		35	
Indiana		38	
Missouri		39	
California		40	
Ohio		41	
Ohio		43	
Ohio		46	
Texas		47	
Georgia		50	
Georgia		51	
Illinois		52	

Location	Investigator	Site	No. of Subjects
New Mexico	(b)(6)	53	(b)(4)
Georgia		54	
Oregon		55	
Georgia		56	
Utah		57	
Texas		58	
Texas		59	
California		61	
Colorado		64	
Colorado		65	
Colorado		66	
Colorado		67	
Virginia		68	
Florida		70	
Nevada		71	
Texas		72	
Pennsylvania		73	
California		74	
Texas		75	
New York		77	
South Carolina		78	
Oklahoma		79	
Nevada		80	
Oklahoma		81	
Oklahoma		82	
Oklahoma		83	
Missouri		84	
Wisconsin		85	
Wisconsin		86	
South Carolina		87	
Wisconsin		88	
California		91	
Alabama		92	

Location	Investigator	Site	No. of Subjects
Indiana	(b)(6)	93	(b)(4)
Alabama		94	

(b)(4)

Table 2. Procedure Setting

Facility Category	Number of Facilities	Percent of Total (N=76)
(b)(4)		

F. Study Demographics

As of May 31, 2009 a total of 584 subjects were enrolled in the ESS305 Post-Approval Study.

Demographic information of the study subjects is provided in the ***Tables 3 - 8***.

Table 3. Ethnic Distribution

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

Ethnicity	Number	Percent of Total
Total	584	100%

Table 4. Race Distribution

Race	Number	Percent of Total
White / Caucasian	(b)(4)	
African-American or Black		
American Indian or Alaska Native		
Asian		
Native Hawaiian or Other Pacific Islander		
Other:		
No Answer / Unknown		
Total	584	100%

Table 5. Highest Level of Education

Education Level	Number	Percent of Total
2	(b)(4)	
3		
4		
5		
6		
7		
8		
9		
10		
11		
High School		
Trade/Vocational School		
Community College		
College		
Post-Graduate		
Declined to state		
No answer provided		
Total	584	100%

Table 6. 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	584	100%

(b)(4)

Table 7. Age Distribution at time of Essure placement

N=584 mean= (b)(4) **Range=** (b)(4)

Age	Number	Percent of Total
(b)(4)		

Table 8. Patient Demographics (N=584)

Variable	Mean	Median	Range	Std deviation
Age	(b)(4)			
Height*				
Weight				
BMI*				
Gravidity				
Parity				

(b)(4)

G. Medical History of Study Subjects

Prior Abdominal/Pelvic Surgery

(b)(4)

Other OB/GYN Conditions that Required Treatment

(b)(4)

Primary Method of Contraception Used

(b)(4)

Table 9. Primary Contraceptive Method

Primary method of contraception prior to Essure procedure	Number of Subjects	Percent of Total (N=584)
(b)(4)		

Primary method of contraception prior to Essure procedure	Number of Subjects	Percent of Total (N=584)
(b)(4)		
Total	584	100%

H. Pre-Procedure Data

(b)(4)

Table 10. (b)(4)

(b)(4)	Number of Procedures	Percent of Total (N=584)
	(b)(4)	
Total	584	100%

Table 11. (b)(4)

(b)(4)	Number of Procedures	Percent of Total (N=357)
	(b)(4)	

(b)(4)	Number of Procedures	Percent of Total (N=357)
(b)(4)	(b)(4)	
Total	357	100%

The use of pre-procedure non-steroidal anti-inflammatory drugs (NSAIDs) is recommended by the Essure instructions for use. ***Table 12***, shows the number of patients that were prescribed NSAIDs prior to the placement procedure.

Table 12. Use of pre-procedure NSAIDs

NSAIDs prescribed pre-procedure?	Number of Procedures	Percent of Total (N=584)
Yes	(b)(4)	
No		
Question not answered/unknown		
Total	514	100%

Table 13, shows the type of NSAIDs prescribed and the number of patients that received each drug. Some patients were prescribed more than one NSAID.

Table 13. Type of pre-procedure NSAIDs prescribed

Type of NSAID	Number of Patients Taking NSAID
(b)(4)	(b)(4)

Type of NSAID	Number of Patients Taking NSAID
Total	524

I. Anesthesia

(b)(4)

Table 14. Predominant Anesthesia Used

Predominant Anesthesia	Number of Procedures	Percent of Total (N=584)
Local anesthesia (with or without oral and/or IM analgesia)	(b)(4)	
IV sedation (with or without local anesthesia or oral analgesia)		
General anesthesia (with or without IV sedation, local anesthesia, or oral analgesia)		
Oral medications		
Total	584	100%

J. Hysteroscope Data

A variety of hysteroscope brands were selected for use in the Essure placement procedure attempts (and non-attempts) as listed in ***Table 15***. The hysteroscope

(b)(4)

Table 15. Brand of Hysteroscope Used

Hysteroscope Brand	Number of Procedures	Percent of Total (N=584)
	(b)(4)	
Total	584	100.0%

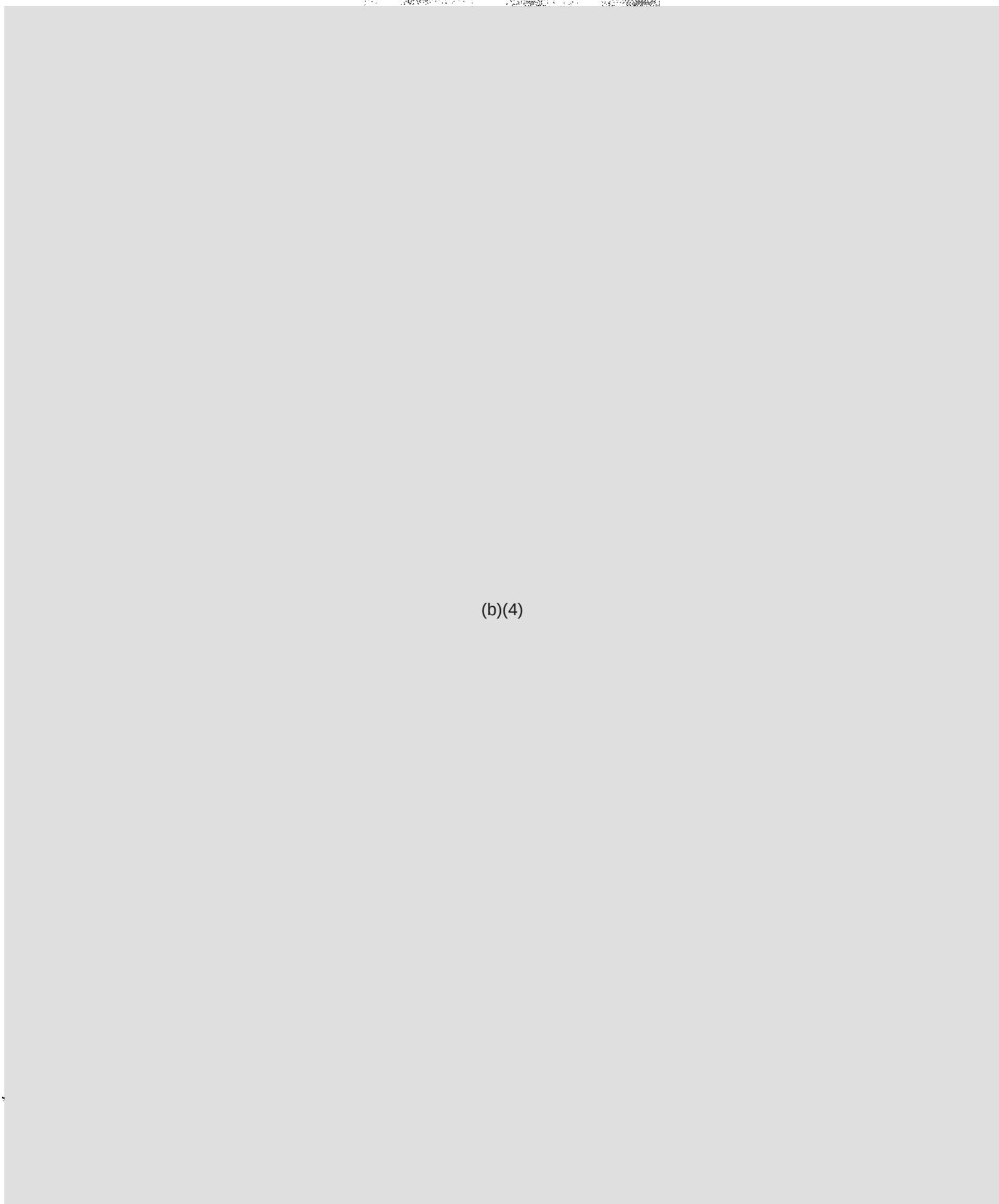
Table 16. Diameter of Hysteroscope Sheath

Hysteroscope Diameter (mm)	Number of Procedures	Percent of Total (N=584)
	(b)(4)	
Total	514	100.0%

K. Micro-insert Placement Data

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

Figure 1: Patient Tree



(b)(4)

Procedure "Non-Attempts"

(b)(4)

Table 17. Placement Procedure Non-Attempts

Patient No.	Reason for non-attempt of placement procedure
(b)(6)	The patient had a vaso vagal episode. The scope was removed. Patient was given Atropine and oxygen. She recovered as expected and was rescheduled for another attempt in the future.
	Poor distension
	Tubal obstruction/spasm. Unusual uterine anatomy: Ostia at right angles
	Ostium not visualized
	Ostium not visualized
	Uterine perforation occurred before entering the uterine cavity towards the left broad ligament.
	Unusual uterine anatomy: internal os extremely stenotic, patient did not want further attempt at dilation due to discomfort

Hysteroscopic Procedure Time (Including Non-Attempts)

(b)(4)

Approval Study (305 Device) and the Pivotal Trial (Gamma Device) is shown in ***Table 18***.

Table 18. Hysteroscopic Procedure Time - comparison with previous studies

Study	N	Average (minutes)	Std. Dev. (minutes)	Median (minutes)	Minimum (minutes)	Maximum (minutes)
PAS 305	584	(b)(4)				
PAS 205	514					
Pivotal Trial	516					

(b)(4)

(b)(4)

Table 19. (b)(4)

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

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

(b)(4)

Placement Failure

(b)(4)

Table 20. Categorization of Placement Failures

Primary reason for placement failure	No. of Patients	Percent of total (N=16)	Patient No.
Ostium not visualized due to unusual uterine anatomy	(b)(4), (b)(6)		
Ostium not visualized			
Tubal obstruction/spasm (with our without lateral tubes and/or device issue)			
Device malfunction			

Primary reason for placement failure	No. of Patients	Percent of total (N=16)	Patient No.
(b)(4)			

Table 21. Causes of Unilateral Placement Failure

Pt. #	Micro-insert Placement		Unilateral Failure Description
	Left	Right	
(b)(6)	Yes	No	Ostium not visualized. Right tubal obstruction/spasm. Right tubal ostia located laterally and covered with film, preventing placement. Right Device bent
	No	Yes	Ostium not visualized
	Yes	No	Tubal obstruction/spasm
	No	Yes	Tubal obstruction/spasm
	Yes	No	Tubal obstruction/spasm, 1st device-bent tip and 2nd device would not release
	No	Yes	Ostium not visualized. Left tubal ostium located laterally, preventing placement. Unusual uterine anatomy: fibroid.
	Yes	No	Tubal obstruction/spasm
	No	Yes	Tubal obstruction/spasm
	No	Yes	Tubal obstruction/spasm
	No	Yes	Ostium not visualized. Left unusual uterine anatomy: uterine septum

Table 22. Causes of Bilateral Placement Failure

Patient No.	Bilateral Failure Description
(b)(6)	Device related failure – Device deployed, tangled, broke and a partial piece of the device was left. Hydrothermal ablation was done after the procedure
	Tubal obstruction/spasm. Left tubal ostium located laterally, preventing placement. Right - History of endometriosis and laparoscopy. Left tube appeared stenotic and felt obstructed. Angle of right ostia prevented insertion, likely related to retroversion of uterus.
	Right tubal obstruction/spasm. Left attempted twice, once button pressed, the wheel would not move and had to pull out

Patient No.	Bilateral Failure Description
(b)(6)	Endometrium prevented proper visualization of both and there was unusual uterine anatomy - bicornuate uterus
	Right ostium not visualized, proceeded to tubal ligation
	Tubal obstruction/spasm

Placement Rates

In this section we calculate the placement rates of the Essure ESS305. Bilateral placement was achieved in (b)(4) subjects. Unilateral micro-insert placement failure occurred in (b)(4) subjects. Bilateral micro-insert failure occurred in (b)(4) subjects.

Micro-insert placement rates are listed in ***Tables 23-24***.

Table 23. Placement Rates – including non attempts (N=584)

Placement Status	Number	Percent
Intent to treat subjects	584	100
Placement Non-Attempts	(b)(4) / 584	(b)(4)
Subjects undergoing placement attempts		
Bilateral Micro-insert Placement	(b)(4) / 584	(b)(4)
Unilateral Micro-insert Placement	(b)(4) / 584	(b)(4)
Bilateral Failure	(b)(4) / 584	(b)(4)

Table 24. Placement Rates - excluding non attempts (N=578)

Placement Status	Number	Percent
Subjects undergoing placement attempts	578	100
Bilateral Micro-insert Placement	(b)(4) / 578	(b)(4)
Bilateral Failure	(b)(4) / 578	(b)(4)
Unilateral Failure	(b)(4) / 578	(b)(4)

Trailing Lengths

(b)(4)

Table 25. Trailing Lengths (expressed as Number of Outer Coils)

Fallopian Tube	Average	Std. Dev.	Median	Minimum	Maximum
(b)(4)					

L. Concomitant Procedures

(b)(4)

Table 26. Concomitant Procedures

(b)(4)

(b)(4)

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

Table 27. Concomitant Procedure Effects

(b)(4)

Device Issues and Malfunctions

Essure device issues were reported in 14 procedures out of 584 procedures included in data analysis as summarized in ***Table 28***. Multiple issues may be reported for one procedure.

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

Table 28. Device Issues and Malfunctions

Patient No.	Lot	Description
(b)(6)		Device did not deploy; was removed and another one placed and deployed successfully. Successful bilateral placement.
		Right device bent. Tubal obstruction/spasm present; tubal ostia located laterally preventing placement. Unilateral placement.
		The tip of the device was slightly bent as it was passed by the introducer, making placement slightly more difficult. Successful bilateral placement.
		Tip of coil bent in black portion of transducer/introducer. Pulled out, bent back and threaded successfully. On the Right the sheath did not retract completely; no green number visible and coil had prematurely unraveled. Had to use a second device and was successful. Successful bilateral placement.
		First attempt at placement of device into right tube was unsuccessful due to malfunctioning of the device. The second device was placed successfully. Bilateral

Patient No.	Lot	Description
		successful placement.
(b)(6)		Device-related failure, Right. First device had a bent tip; second device would not release. Tubal obstruction/spasm on Right. Unilateral placement.
		Device-related failure. No placement.
		Tubal obstruction/spasm on Right. Attempted Left twice. Once wheel "advanced" or button pressed, the wheel would not move and had to pull out. No placement.
		Right tube cannulated without problem. When coils were released, part of the insert did not detach and was left behind in center of coils. Reported to ESSURE rep. Successful bilateral placement.
		First device for Left tube was bent at tip upon entering the uterine cavity. Second device was then used and a replacement device (with different Lot #) was used for the Right tube. Successful bilateral placement.
		Device failure - implants were elongated out of package and unable to cannulate tubes. Second package opened and tubes cannulated without difficulty. Successful bilateral placement.
		Misfire of the spring in device prior to pressing the button. Device removed with biopsy graspers, and a different device was used. Successful bilateral placement.
		Both devices malfunctioned in first kit and were unable to be placed. Both devices deployed properly with the second kit. Successful bilateral placement.
		The Dacron was visible with the first coil release. The coil pulled out when removing the guide and was retrieved and another coil was inserted without incident. Successful bilateral placement.

M. Safety of Micro-insert Placement Procedure

Adverse Events

Adverse events that occurred during and after the Essure placement procedure have been reported in 6/584 subjects included in the analysis (.01%). All reported events were minor with the exception of Patient (b)(6) The patient was hospitalized after hysteroscopy resulted in a uterine perforation by the hysteroscope. The Essure device did not cause the injury to the patient. None of these events represent unanticipated adverse device effects. ***Table 29*** summarizes all events and the patient management for each.

Table 29. Adverse Events

Patient No.	Adverse Event / Complication
(b)(6)	Irregular bleeding from (b)(4) Physician deemed this unrelated to the device and patient recovered with medication.
	Patient fainted and experienced emesis as she was leaving the office post-procedure. Her symptoms resolved at the time of discharge.
	Inconsequential uterine perforation from dilator occurred prior to hysteroscope insertion. No sequelae.
	Although no issues were encountered during the procedure, patient later experienced a tubal spasm and vasovagal episode. Patient rested on her side with a cool cloth for about 10 minutes post-procedure.
	Patient experienced a vasovagal episode when lying down during lidocaine injection. She also experienced nausea with vomiting, but relaxed for 5 minutes and was able to continue with the procedure. Due to menses 10u vasopressin was injected into cervix.
	Hysteroscopy resulted in uterine perforation before reaching the uterine cavity. Patient was hospitalized and a diagnostic laparoscopy performed.

N. Clinical Trial Conduct

(b)(4)

The ESS305 Post-Approval Study protocol was previously submitted in PMA P020014 Supplement 12 and was modified through PMA Supplement 18. A reference copy of the final version of the protocol is included in this report in ***Exhibit G***.

O. Study Deviations and Exclusions

Study Deviations

(b)(4)

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

Sponsor Deviations

(b)(4)

Study Exclusions

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

EXHIBIT A: STUDY SITES AND PHYSICIANS

Exhibit A. ESS305 Post-Approval Study Sites and Participating Physicians

The table below lists each enrolling site/physician participating in the ESS305 Post-Approval Study.

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
1	(b)(6)		
2			
3			
4			
6			
7			
8			
9			
10			
11			
12			
13			

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
14	(b)(6)		
15			
16			
18			
19			
20			
23			
24			
25			
26			
27			
28			
29			

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
30			
31			
32			
33			
34			
35			
38		(b)(6)	
39			
41			
43			
40			
46			
47			

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
50	(b)(6)		
51			
52			
53			
54			
55			
56			
57			
58			
59			
61			
64			
65			
66			

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
67	(b)(6)		
68			
70			
71			
72			
73			
74			
75			
77			
78			
79			
80			
81			
82			

SITE #	Physician Name	Site Address	Training Institute, Community Hospital, Surgical Center or Physician Office
83	(b)(6)		
84			
85			
86			
87			
88			
91			
92			
93			
94			

EXHIBIT B: PROCEDURES REQUIRING ADDITIONAL HYSTEROSCOPY TIME

Exhibit B. Procedures requiring additional hysteroscopy time

Patient	Proc Time	Thru Channel	Placement Status	Addl Procedures	Before Or After	Impact on Essure	Reasons for Increased Procedure time
(b)(4)	50	Yes	Unsuccessful, No placement	No	N/A	N/A	Tubal obstruction/spasm - device wheel would not move, had to pull out
	45	Yes	Unsuccessful, No placement	Hydrothermal Endometrial Ablation	After	Yes	Additional Procedure Time
	29	Yes	Unsuccessful, No placement	No	N/A	N/A	Unusual uterine anatomy-Bicornuate Uterus - Endometrium prevented proper visualization
	26	No	Unsuccessful, No placement	No	N/A	N/A	Poor distension
	22	Yes	Unsuccessful, No placement	No	N/A	N/A	Tubal obstruction/spasm,~Both
	22	No	Unsuccessful, No placement	No	N/A	N/A	Stenotic cervix and discomfort - Unusual uterine anatomy ~internal os extremely stenotic pt did not want further attempt at dilation due to discomfort.
	24	Yes	Unilateral Placement	No	N/A	N/A	Tubal obstruction/spasm, Right
	27	Yes	Unilateral Placement	No	N/A	N/A	Tubal obstruction/spasm, Left
	75	Yes	Bilateral Success	No	N/A	N/A	The patient was in the luteal phase of her menstrual cycle, making it more difficult to visualize the ostia. As a result, the hysteroscopic portion of the procedure took longer than expected.
	44	Yes	Bilateral Success	No	N/A	N/A	No reason given
	38	Yes	Bilateral Success	No	N/A	N/A	Initially felt that first device would not deploy. On further inspection, it appears the first device was placed distally as there was no coil on the device once removed from the uterus.

Patient	Proc Time	Thru Channel	Placement Status	Addl Procedures	Before Or After	Impact on Essure	Reasons for Increased Procedure time
(b)(4), (b)(6)							

Patient	Proc Time	Thru Channel	Placement Status	Addl Procedures	Before Or After	Impact on Essure	Reasons for Increased Procedure time
(b)(4), (b)(6)							

EXHIBIT C: CONCOMITANT PROCEDURES

Exhibit C. Concomitant Procedure Data

Patient	Placement Status	Primary Reason for Failure	AEs	Additional Procedures	Prior to OR after ESSURE	Impact on Essure Procedure
(b)(4)	Non Attempt	Unusual uterine anatomy	Uterine perforation by scope	Diagnostic Laparoscopy , BTL with Filshie Clips	Prior	Essure could not be performed
	Bilateral Failure	Ostium not visualized	No	Laparoscopic tubal ligation	After	No
	Bilateral Success	N/A	No	Diagnostic Laparoscopy	After	No
	Bilateral Success	N/A	No	IUD removal	Prior	No
	Bilateral Success	N/A	No	IUD removal	Prior	No
	Bilateral Success	N/A	No	IUD removal	Prior	No
	Bilateral Success	N/A	No	Labia minora mass removal	After	No
	Bilateral Success	N/A	No	Pap smear	Prior	No
	Bilateral Success	N/A	No	Removal of synechia covering left ostia - Polyp grasper used to lyse adhesions and reveal ostia on left side	Prior	Additional equipment and additional procedure time
	Bilateral Success	N/A	No	Umbilical herniorrhaphy	After	No
	Bilateral Success	N/A	No	Thermachoice (uterine balloon therapy)	After	No
	Bilateral Success	N/A	No	Thermachoice (uterine balloon therapy)	After	No

Patient	Placement Status	Primary Reason for Failure	AEs	Additional Procedures	Prior to OR after ESSURE	Impact on Essure Procedure
(b)(4), (b)(6)						

Patient	Placement Status	Primary Reason for Failure	AEs	Additional Procedures	Prior to OR after ESSURE	Impact on Essure Procedure
(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)			No	Deployment issue with device, therefore it was removed and another one placed and deployed.	Detachment difficulty: after micro-insert was positioned in the ostium the full sequence to deploy was performed. The micro-insert did not release from the delivery catheter due to the tip of the scope being too close to the gold marker band ; not enough green catheter between the fold band and scope tip. Bilateral placement achieved and no patient injury.
			No	Right device bent secondary to tubal obstruction/spasm; tubal ostia located laterally preventing placement.	The failure to place the device was due to poor visualization and lateral tubes. Device was bent in the process. Unilateral placement and no patient injury.
			No	Device tip was slightly bent as it passed through the introducer which made placement slightly more difficult.	Bilateral placement achieved and no patient injury.
			No	Tip of coil bent in black portion of transducer/introducer. Pulled device out, bent back and threaded successfully. On the Right the sheath did not retract completely; no	Bilateral placement achieved and no patient injury.

Patient No. and Physician	Lot No. and AR No.	Date of Occurrence	Device Returned ?	Issue or Malfunction Description	Evaluation Results
(b)(4), (b)(6)				green number visible and coil prematurely unraveled. Used a second device and was successful.	
			No	First attempt at placement of device into Right tube was unsuccessful due to malfunctioning of the device. The second device was placed successfully.	Bilateral placement achieved and no patient injury.
			No	Device-related failure, Right. 1st device - bent tip; 2nd device would not release. Tubal obstruction/spasm also present.	Deployment difficulty (b)(4) and bent tip on the introducer ((b)(4) Unilateral placement and no patient injury.
			No	Device-related failure.	MD inserted catheter to the black marker band with no resistance. MD then visually confirmed correct placement of inner green catheter and gold band outside of the ostia. MD depressed button and thumbwheeled back to a hard stop. The device deployed, but the coils/device tangled into a ball located proximally in the ostia. The device visually did not appear to be inserted into the tube. MD elected to use graspers to remove the device, but the device broke apart and she met resistance with removing the coils. She elected to leave in place a partial device that had no center rod with Dacron. MD discontinued the procedure. Bilateral placement was not achieved. There was no patient injury.

Patient No. and Physician	Lot No. and AR No.	Date of Occurrence	Device Returned ?	Issue or Malfunction Description	Evaluation Results
(b)(4), (b)(6)			No	Tubal obstruction/spasm on Right. Attempted Left twice. Once wheel "advanced" or button pressed, the wheel would not move and had to pull out.	Deployment difficulties: physician states there were deployment difficulties with all five devices; button would no depress after visualizing green and orange markers and therefore second wheelback could not be completed. Bilateral placement was not achieved. No patient injury.
			No	Right tube cannulated without problem. When coils were released, part of the insert did not detatch and was left behind in center of coils. Reported to ESSURE rep.	Deployment difficulty: Right tube cannulated without problem. When coils were released, part of the insert did not detach and was left. Bilateral placement achieved and no patient injury.
			No	1st device for Left tube was bent at tip upon entering the uterine cavity. Second device was used and a replacement device (with different Lot #) was used for the Right tube.	Bilateral placement achieved and no patient injury.

Patient No. and Physician	Lot No. and AR No.	Date of Occurrence	Device Returned ?	Issue or Malfunction Description	Evaluation Results
(b)(4), (b)(6)			No	Device failure - implants were elongated out of package and unable to cannulate tubes. Second package opened and tubes cannulated without difficulty.	(b)(6) tried to cannulate the first tube and he thought the device did not look like it normally did, but he tried to cannulate and the device kept bending. He thought the delivery catheter was rolled back possibly and tried to roll it back and the thumbwheel did turn. He pulled that device and tried another one. The same thing happened again. Another box was opened and successful bilateral placement was achieved with no problem. No patient injury.
			No	Spring misfired in device prior to pressing the button. Device removed with biopsy graspers, and a different device was used.	Bilateral placement achieved and no patient injury.
			No	Both devices malfunctioned in first kit and were unable to be placed. Both devices deployed properly with the second kit.	First Essure device easily inserted through hysteroscope and into uterine cavity, but spontaneously deployed. MD never thumbwheeled back. Coils were visibly uncoiled as soon as it was in the uterine cavity and attempt to cannulate tube was aborted. Second Essure device was inserted through scope and the same thing occurred. Scope was removed and channel cleaned with the grasping forceps. A part of Essure inserted (from first or second device) was lodged in operative chamber and was removed. Hysteroscope was inserted back in patient and new introducer placed. New lot of Essure inserts were placed bilaterally without difficulty and there was no patient injury.

Patient No. and Physician	Lot No. and AR* No.	Date of Occurrence	Device Returned ?	Issue or Malfunction Description	Evaluation Results
(b)(4), (b)(6)			No	The dacron was visible in the first coil release. The coil pulled out when removing the guide and was retrieved. Another coil was inserted without incident.	Bilateral placement achieved and no patient injury.

EXHIBIT E: PRIOR ABDOMINAL SURGERY

Exhibit E. Prior Abdominal Surgery

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	1	Endometrial Cryoablation	(b)(4), (b)(6)	
	1	C-Section		
	1	Salpingostomy		
	1	Appendectomy		
	1	Cholecystectomy		
	1	Cholecystectomy		
	1	Cholecystectomy		
	2	D&C x 2		
	1	HTA		
	1	D&C for MAB		
	1	Myomectomy		
	1	cholecsytectomy		
	1	Gastric Bypass		
	1	Removal of uterien septum		
	1	LEEP		
	1	D&C		
	1	LEEP		
	1	D&E		
	1	LEEP		
	1	Laparoscopic Gall Bladder Surgery		
	1	Ovarian cystectomy		
	1	Cholecystectomy		
	1	Appendectomy		
	1	Diagnostic laprascopy		
	1	Dx Hysteroscopy DxLaparoscopy		

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	1	Diagnostic Laparoscopy	(b)(4), (b)(6)	
	2	Diagnostic Laparoscopy		
	1	Gastric Bypass		
	1	LEEP		
	1	Abdominal cerclage		
	1	Appendectomy		
	1	Appendectomy		
	2	Laproscopic Cholecystectomy		
	1	C-Section		
	1	Gastric bypass		
	1	Ovarian Cyst		
	1	C-Section		
	1	Gallbladder		
	1	gallbladder		
	1	Gallbladder		
	1	Ablation		
	1	D&C		
	1	Umbillical Hernia		
	1	Gastric Bypass		
	2	Cholecystectomy		
	1	Lapband Surgery		
	1	Laparoscopy		
	2	laparotomy		
	1	Appendectomy		
	1	Tubal ligation reversal		
	1	Myomectomy		
	1	Laparoscopic appendectomy		

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	2	Cholecystectomy	(b)(4), (b)(6)	
	3	Gastric bypass		
	4	Gastrectomy		
	1	Cholecystectomy		
	1	Myomectomy		
	1	Cholecystectomy		
	1	Appendectomy		
	2	Diagnostic laparoscopy		
	1	D&C		
	1	Cholecystectomy		
	1	Gallbladder removal		
	2	Tubal reversal		
	1	Appendectomy		
	1	Appendectomy		
	2	Cholecystecomy		
	1	Cryotherapy		
	1	Cholecystectomy		
	1	Cholecystectomy		
	1	D & C		
	1	Laparotomy partial salpingectomy		
	1	Laparoscopy		
	1	Tummy Tuck		
	1	Laparoscopy		
	1	Cystocele repair		
	1	Ovarian cystectomy		
	1	C-Section		
	2	C-Section		

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	1	Laparoscopic Cholecystectomy	(b)(4), (b)(6)	
	1	C-Section		
	1	D&C		
	1	Dilitation and curretage		
	1	C-section		
	2	C-section		
	3	C-section		
	1	Appendectomy		
	2	Laparoscopy		
	1	Appendectomy		
	1	Diagnostic Laparoscopy		
	1	Laparoscopic fulguration of endometriosis		
	1	Cearean Section		
	1	Apppendix		
	2	Gallbladder		
	1	Gastri cbypass		
	2	Laparoscopic Cholecystectomy		
	1	C-Section		
	2	C-Section		
	1	Tubal Reanastomosis		
	1	Cesarean Section		
	1	Cesarean Section		
	2	Cesarean Section		
	3	Cesarean Section		
	1	Cesarean Section		
	1	Appendectomy		
	1	Laparoscopy		

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	2	Laparoscopy Tubal Ectopic	(b)(4), (b)(6)	
	1	Splenectomy		
	1	Cholecystectomy		
	1	Gastric Bypass Surgery 2002		
	1	Partial Colectomy		
	1	Appendectomy		
	1	C-Section		
	1	C-Section		
	2	Laproscopy		
	3	C-Section		
	1	Cholecystectomy		
	1	Laser Laproscopy		
	1	Cesarean section		
	1	Cesarean section		
	1	Cesarean section		
	1	C-Section		
	1	Lap Band		
	1	Appendectomy		
	2	Cesarean Section		
	3	Cesarean Section		
	1	Duodenal switch		
	1	Cerclage		
	1	Roux N-Y		
	1	Removal of endometrioma		
	2	Removal of endometrioma		
	1	Tummy tuck		
	1	Laparoscopic Cholecystectomy		

Patient	Surgery #	Prior Abdominal Surgery	Date of Onset	Date of Resolution
(b)(6)	1	C-Section	(b)(4), (b)(6)	
	1	Exploratory Lap		
	2	Cholycystectomy		
	3	C-Section		
	4	C-Section		
	5	C Section		
	1	Gallbladder		
	1	Gallbladder		

EXHIBIT F: PROTOCOL DEVIATIONS

Exhibit F. Protocol Deviations

Patient #	Protocol Deviation Description
(b)(4), (b)(6)	

Patient #	Protocol Deviation Description
(b)(4), (b)(6)	

Patient #	Protocol Deviation Description
(b)(4), (b)(6)	

Patient #	Protocol Deviation Description
(b)(4), (b)(6)	

EXHIBIT G: CLINICAL STUDY PROTOCOL AND CASE REPORT FORMS

Conceptus

Post-Approval Clinical Study Protocol:
Placement of the ESS305 Essure® System

VERSION (b)(4)

Sponsor:
Conceptus Incorporated
331 E. Evelyn Ave.
Mountain View, CA 94041

Telephone 650-962-4000

REVISION HISTORY

Version Number	Description of Change	Effective Date
Version	(b)(4)	May 30, 2007
Version		June 9, 2007
Version		June 12, 2007
Version		June 12, 2007
Version		August 7, 2008

Table of Contents

1. Background

The Essure System is comprised of a micro-insert attached to a delivery wire, held in the wound down position by the release catheter. The entire assembly is sheathed within a delivery catheter. This system is attached to a handle that facilitates micro-insert delivery and deployment. Conceptus has made several modifications to the currently marketed

(b)(4)

Table 1. Summary of Principal Design Changes of Essure System ESS305

Modification	Benefits
(b)(4)	

The ESS305 System and has been subjected to bench testing to demonstrate its comparability to the existing ESS205 System. The results of this bench testing were used to support a Pre-Market Application Supplement (#P020014/S12) and submitted to the Food and Drug Administration.

2. Study Purpose

The purpose of this post-approval clinical study is to determine the following:

2.1 Bilateral placement of the ESS305 micro-insert at first attempt;

2.2 Comparison of bilateral placement success between Newly Trained physicians and Experienced physicians

2.3 Identification of factors predictive of failure to achieve bilateral placement of the ESS305 micro-insert at first attempt;

2.4 Evaluation of aspects of the ESS305 design that may impact bilateral placement rate;

2.5 Hysteroscopy time to perform the procedure

2.6 Adverse device effects; and

2.7 Adverse procedure events.

The data will be used to evaluate training procedures and update labeling as required.

3. Basic Study Design

This study is designed to collect demographic and micro-insert placement data on a minimum of 800 women from 80 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 80 physicians are needed to reach a total of 800 women, up to (b)(4) physicians will be enrolled in this study in the event that not all physicians complete a total of (b)(4) cases, or do so on a timely basis. Enrollment in this study will cease after data is available from 80 physicians who have provided data regarding (b)(4) cases of Essure placement attempt.

Investigator enrollment in this study will be limited to no more than (b)(4) physicians from any one state and no more than (b)(4) newly trained physicians and/or (b)(4) experienced physicians from any one institution. In addition, no more than (b)(4) of the physicians will represent (b)(4).

(b)(4)

Table 2. Type and number of physician investigators required

Essure placement experience of enrolled Physicians	Number of physicians required to participate	Number of patients
Newly trained and certified to perform placement, but with no commercial experience beyond preceptored training cases	(b)(4)	
Certified and having at least (b)(4) commercial placement attempts (i.e. "experienced" physicians)		
Totals:	**80** (minimum) **86** (maximum)	**800** (minimum) **860** (maximum)

3.1 Newly Trained Physicians

Up to (b)(4) physicians in (b)(4) in the United States who complete the (b)(4) of the training program and (b)(4) (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 preceptoring portion includes training on commercial patients with an experienced Conceptus representative in attendance until physician competence is demonstrated (typically 3-5 cases, but could be higher).

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 (b)(4) women will be enrolled in order to obtain data on (b)(4) women with an actual placement attempt.

3.2 Experienced Physicians

Up to (b)(4) physicians in (b)(4) in the United States who have previously completed the Essure training program and have commercial experience with at least (b)(4) micro-insert attempts 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 have previous experience in Essure micro-insert placement with at least (b)(4) micro-insert placement attempts.

The enrolled physicians will then collect demographic and micro-insert placement data on the first cases performed after ESS305 training is complete according to the training plan in ***Appendix D***, 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 (b)(4) women will be enrolled in order to obtain data on (b)(4) women with an actual placement attempt.

3.3 Study Site Selection Plan

Study sites will be selected in the United States in (b)(4) to achieve an appropriate enrollment rate of study subjects. Sites will be selected based on (b)(4) levels of physician experience with Essure placement as shown in ***Table 3*** below. A minimum of (b)(4) sites with a total of (b)(4) newly trained (but without commercial experience) physicians will be enrolled. (b)(4) alternate sites may be enrolled with a maximum of (b)(4) newly trained physicians in order to achieve micro-insert placement attempt in a total of (b)(4) patients, the minimum number required. In addition, a minimum of (b)(4) sites with a total of (b)(4) "experienced" physicians will be enrolled. (b)(4) alternate sites may be enrolled with a maximum of (b)(4) experienced physicians in order to achieve micro-insert placement attempt in a total of (b)(4) patients, the minimum number required.

Physician enrollment in this study will be limited to no more than (b)(4) physicians from any one state and no more than (b)(4) physicians from any one institution. In addition, no more than (b)(4) of the physicians will represent (b)(4) (b)(4)

Table 3. Study site selection criteria

Minimum # of physicians required to participate	Number of Sites	Type of setting or facility	Maximum # Physicians per State	Maximum # Physicians per site
A. Physicians newly trained and certified to perform placement, but with no commercial experience beyond preceptored training cases				
(b)(4)				
B. Physicians that have previously completed Essure training and having at least 25 commercial placement attempts (i.e. "experienced" physicians)				
(b)(4)				
Totals:				
80 (minimum) **86** (maximum)	**40** (minimum) **44** (maximum)		(b)(4) (maximum)	(b)(4) (maximum)

A pre-investigation meeting will occur with each potential study site in order to orient the prospective investigator and staff to the Post Approval Study, applicable regulations and requirements, expectations of the study, including the numbers and time frame for patient enrollment, patient selection, informed consent, required clinical data and record keeping, and so forth. The prospective study site will be evaluated to ensure that it has an adequate patient base and can provide sufficient staff and documentation support to conduct the study properly.

No study site may begin patient enrollment in this study until the following documents are received by Conceptus:

- (b)(4)

3.4 Projected Timeline

(b)(4)

Table 4a. Estimated timeline of post approval study

Clinical Study Milestone	Expected Completion Date
Initial Site Enrollment with IRB approval	August 2007
86th Site Enrolled with IRB approval	August 2008
Initial Patient Enrollment	September 2007
100th Patient Enrolled	December 2007
200th Patient Enrolled	February 2008
400th Patient Enrolled	May 2008
600th Patient Enrolled	December 2008
860th Patient Enrolled	October 2009
Final report prepared	November 2009
Final report submitted to FDA	December 2009

Table 4b. Expected number of Investigators and study subjects enrolled by month	Expected # of Investigators enrolled (cumulative)	Expected # of Patients enrolled (cumulative)
(b)(4)		

4. Study Endpoints

The study endpoints are as follows:

4.1 Bilateral micro-insert placement rate at first attempt;

4.2 Comparison of bilateral placement success between Newly Trained physicians and Experienced physicians
4.3 Identification of factors predictive of micro-insert placement failure;
4.4 Evaluation of aspects of the ESS305 design that may impact bilateral placement rate;
4.5 Hysteroscopy time to perform the procedure;
4.6 Adverse device effects; and
4.7 Adverse procedure events.

The nature and frequency of adverse device effects or adverse procedural events that may occur during or after placement procedure up to discharge will be assessed.

(b)(4)

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

(b)(4)

5. Designated Person

The (b)(4) will be responsible for the data analysis and report preparation.

6. Inclusion and Exclusion Criteria

All inclusion and exclusion criteria from the Instructions for Use approved under PMA Supplement #P020014/S12 will apply.

Additional inclusion criteria:

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

Additional exclusion criteria:

- Women who present with any other medical complaints, conditions or symptoms unrelated to the Essure placement procedure that require concomitant hysteroscopic diagnosis or therapy. Excluding these candidates will allow Conceptus to accurately measure the hysteroscopy time to perform the Essure placement procedure using the ESS305 device.

7. Adverse Events

An adverse event is any undesirable experience (sign, symptom, illness, abnormal laboratory value, or other medical event) occurring to a patient, whether or not considered related to the investigational product(s) or drug regimen prescribed as part of the protocol, that appears or worsens during a clinical study.

Adverse event information will be collected throughout the study. Adverse events will be recorded on the case report forms by the Investigator or study coordinator. Event, date of onset, severity, duration, and relationship to device or prescribed drug regimen will be recorded on the appropriate case report form. Any adverse events will be monitored until they are adequately resolved or explained. The proportion of subjects who experience a procedure-related adverse event or adverse device effect, as judged by the Investigator, will be determined.

7.1 Serious Adverse Events

The Investigator must first decide whether each event meets the definition of a "serious" adverse event. The regulatory definition of a serious adverse event is an event that is fatal or life-threatening, results in persistent or significant disability, requires intervention to prevent permanent impairment/damage, or an event that results in congenital anomaly, re-admission or prolongation of hospitalization.

All serious, expected or unexpected, device or procedure-related adverse events and deaths must be reported immediately (within 24 hours) by telephone to the relevant IRB and to Conceptus, confirmed in writing in 5 working days by the Investigator and recorded on the case report form. All other serious adverse events must be reported to the IRB, Conceptus, and the Data Safety Monitoring Board (defined in ***Section 8*** below) within 24 hours of knowledge of event. Reports relating to the patient's subsequent medical course must be submitted to Conceptus until the event has subsided or, in case of permanent impairment, until the event stabilizes and the overall clinical outcome has been ascertained.

7.2 Unanticipated Adverse Device Effects

Unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. These events must be reported to the IRB, Conceptus, and the Data Safety Monitoring Board (defined in ***Section 8*** below) within 24 hours of knowledge of event. Reports relating to the patient's subsequent medical course must be submitted to Conceptus until the event has subsided or, in case of permanent impairment, until the event stabilizes and the overall clinical outcome has been ascertained.

7.3 MDR Reportable Events

Because this is a post-approval study, the Essure System ESS305 is subject to Medical Device Reporting (MDR) regulations. Conceptus will review all serious adverse events and unanticipated adverse device effects and determine their reportability to FDA according to 21 CFR 803 "*Medical Device Reporting*." Reporting MDR's to FDA is required when the manufacturer (Conceptus) becomes aware of information that reasonably suggests that a marketed device has or may have caused or contributed to a death, serious injury or long-term pain necessitating surgical intervention, or has malfunctioned, and that the device or a similar device marketed by the manufacturer would be likely cause or contribute to a death or serious injury if the malfunction were to recur.

7.4 Device Failures and Malfunctions

All device failures and malfunctions will be documented on the Case Report Forms and reported in the clinical results. Essure System devices that fail or malfunction will be returned to Conceptus for analysis after appropriate decontamination per Study Site guidelines.

7.4.1 Device Failure

A device has failed if it does not perform according to labeling and negatively impacts the treatment while used according to the labeling.

7.4.2 Device Malfunction

A device malfunction is an unexpected change to the device that is contradictory to the labeling and may or may not affect device performance.

8. Interim Analyses and Stopping Rules

8.1 Data Safety Monitoring Board

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

9. Data collection

Data will be collected using standardized Case Report Forms (CRFs). The Physician or his/her designee will enter the relevant information onto the case report forms shown in ***Appendix B***.

(b)(4)

9.1 Site Data Monitoring and Quality Control

(b)(4)

10. Study Procedure

Micro-insert placement will be performed according to the Instructions for Use (IFU) approved under the Essure PMA Supplement #P020014/S12 and shown in ***Appendix C***.

10.1 Reports

Investigators are required to prepare and submit to Conceptus complete, accurate and timely reports on this investigation when necessary according to ***Table 5*** below.

(b)(4)

(b)(4)

11. Informed Consent and Ethical Considerations

The product under study, Essure System ESS305, is approved for commercial use. This study will be performed on patients who desire permanent contraception.

Prior to taking part in the study, the Investigator or his/her designee will fully inform the patient of the potential risks and benefits of study participation, according to the Informed Consent approved by the overseeing Institutional Review Board (IRB). A sample Informed Consent form is contained in **Appendix E** of this Protocol. The patient will be given the opportunity to discuss fully any questions she may have. Failure to provide informed consent renders the patient ineligible for the study.

Conceptus representatives may be present during the Micro-insert placement procedures. It is the responsibility of the Investigator to inform patients that Conceptus representatives may be present during Micro-insert placement. The informed consent must contain wording to this effect. Conceptus representatives are not present to make medical decisions. All medical decisions are the responsibility of the Investigator, and not of the Conceptus representatives.

11.1 Institutional Review Board (IRB) Information

This protocol and the informed consent must be reviewed and approved by the appropriate IRB where the trial is to be conducted before enrollment of patients. Changes to the protocol that may increase the risk or present new risks to the patient, or may adversely affect the validity of the trial, must be approved in writing by Conceptus, the IRB, and the FDA before the change is made.

(b)(4)

IRB approval to participate in this trial is required from each institution participating in this investigation. Prior to patient enrollment, a signed copy of the IRB Approval Form (See Attachment H), or a signed copy of the IRB approval letter addressed to the investigator must be submitted to Conceptus certifying trial approval. Investigators are responsible for submitting and

obtaining initial and continuing review (at intervals not greater than once a year) of the trial by their IRB.

12. Deviations from Protocol

(b)(4)

13. Training

13.1 Study Site Training

(b)(4)

13.2 Physician Procedure Training

New and experienced physicians will be trained on the differences between the new ESS305 design and the currently available ESS205 Essure System and placement procedure steps according to the training plan in ***Appendix D***.

14. Risks and Benefits

Following are the potential risks associated with long-term wearing of the Essure System and the placement procedure, based on clinical trials of the current catheter an previous designs. These risks may be greater or less with the ESS305 Essure System, and risks not encountered with the current catheter may occur with the new design.

14.1 Risks Associated with the Essure Placement

(b)(4)

(b)(4)

14.2 Risks Associated with Essure Micro-insert Wearing

(b)(4)

14.3 Risks Associated with Follow-up Procedures

(b)(4)

14.4 Risks Associated with Potential Future Procedures

(b)(4)

14.5 Unknown Risks

There is the potential that unknown risks exist.

14.6 Potential Benefits

There is no direct benefit to the patient. However, there is a potential benefit to other women that may have Essure placement using this design in the future based on results from research studies such as this.

15. Records and Reports

15.1 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

15.2 Content and timing of reports

For the first two years of the study, an interim report will be submitted every six months from the date of commencement of the study while the study is ongoing. Further interim reports will follow annually while the study is ongoing. A final report will be submitted to FDA within 3 months of study completion. The report(s) will include the information relating to study progress and the Study Endpoints outlined in Section 4 above.

16. Statistical Analysis and Reporting of Results

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

17. Financial Considerations

(b)(4)

17.1	
17.2	(b)(4)

Note: Appendices omitted.

18. Physician Signature

The Physician will sign the following statement, after reviewing the protocol. I have carefully read and I understand the provisions of protocol, and I agree to follow it in every detail. Furthermore, I understand that any changes to the protocol must be pre-approved by Conceptus, Inc. and the reviewing Institutional Review Board, if applicable. All data for this study will be provided to Conceptus, Inc. and remains the sole property of Conceptus. I agree that any presentation or publication of study data will be pre-approved by Conceptus, Inc. I affirm that the data used in the research will be stored safely and kept confidential, and will only be used for the purpose for which it has been approved.

_____ _____

Physician's Signature Date

Pages 88 through 100 redacted for the following reasons:
- -
(b)(4)-Trade Secret/Confidential Commercial Information
Case Report Forms
(b)(4)-Trade Secret/Confidential Commercial Information
Draft Information-Case Report Form

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P020014/R24/A1

Makers of Essure•

September 18, 2009

U S Food & Drug Administration
Center for Devices and Radiological Health
Office of Surveillance and Biometrics
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

SEP 22 2009

Re PMA P020014, Report #24, Amendment 1
Conceptus Essure® System for Permanent Birth Control

Dear Drs Loyo-Berrios and Marinac-Dabic

This amendment is to provide additional information in response to FDA questions in a letter dated September 11, 2009 This is Amendment #1 to submission PMA P020014, Report 24 FDA's comments are repeated below in bold with Conceptus' response following in normal text

1

(b)(4)

ESS305 Post-Approval Study Conceptus will submit a supplement to update labeling based upon this placement rate summary report

The difference in placement rates across studies (1%) was small and clinically not meaningful

Table 1 Placement Rate Comparison for ESS205 & ESS305 Study

Study	S/N (%)	Comment
ESS205		Of the 15 unilateral placements, 6 were intentional
ESS 305		Current study

2

(b)(4)

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

Please find three paper copies of the submission enclosed 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 650 962 4078, by fax at 650 962 5194, or by email at rachelle_acuna-narvaez@conceptus com Thank you for your continued review of this report

Warm regards,

Rachelle Acuña-Narvaez
Senior Regulatory Affairs Associate
Conceptus, Inc
331 East Evelyn Ave
Mountain View, CA 94041

Exhibit.
Exhibit 1 - Placement Rate Summary ESS305 Post-Approval Study

Conceptus

PLACEMENT RATE SUMMARY: ESS305 POST-APPROVAL STUDY

Ed Yu
Director of Clinical and Regulatory Affairs
Conceptus Incorporated

Daniel Cher
Consulting Statistician
Wild Iris Consulting LLC
Palo Alto, CA 94303

Table of Contents

1. Methods

1.1. Study Purpose

The ESS305 Post-Approval Study (ESS305 PAS) was a study of placement rates of the ESS305 model of the Essure System in experienced and newly trained physicians Differences between the ESS305 and the previous model of the device (ESS205) are discussed in **Table 1** The primary purpose of the study was to determine that placement rates using a modified delivery system were as good as those observed using the previous model of the Essure device This study was conducted in accordance with the post-approval requirements for PMA P020014/S12, as modified by Reports 15, 21, 22 and Supplement 18 Details of the study can be found in the study protocol and the final study report (previously submitted to FDA as PMA P020014/R24) This document describes study outcomes focusing on statistical analysis that addresses the study's main questions

Table 1 Descriptions of modifications made to the ESS205 device in the ESS305 model

	Modification	Benefits
1	(b)(4)	
2		
3		
4		
5		

6	(b)(4)

1.2. Physician Participants

Physician participants were (b)(4) newly trained physicians and (b)(4) experienced physicians practicing in the United States. All physicians were obstetricians and/or gynecologists. A newly trained physician is defined as a physician who has recently undergone Essure device training and has performed (b)(4) cases under the direction of a proctor or preceptor. An experienced physician is defined as a physician who has the same training as a newly trained physician but who has performed (b)(4) Essure placements in commercial practice. In the study, physicians were asked to enroll (b)(4) subjects each.

(b)(4)

1.3. Recruitment

Study subjects were recruited through the enrolling physicians' offices. Eligible participants were women seeking permanent contraception. Subjects were recruited according to all inclusion and exclusion criteria from the Instructions for Use approved under the Essure PMA (P020014/S12). Additional key inclusion criteria included: 1) subject believed to have (b)(4) viable fallopian tubes, and 2) subject signed an IRB-approved informed consent. Primary exclusion criteria were: 1) subject known to have PTO in one or more tubes, 2) subject had prior tubal sterilization procedure, 3) subject had known unicornuate uterus, and 4) subject was pregnant or possibly pregnant. A list of the inclusion/exclusion criteria is included in the study protocol (see P020014/R24).

1.4. Treatment

Micro-insert placement was performed according to the Instructions for Use (IFU) approved under PMA P020014/S12.

1.5. Follow-up

Patient follow-up extended only through the end of device placement. No long-term follow-up was conducted as part of this study.

1.6. Definitions

Outcomes as they relate to the procedure are defined below:

- **Rate of non-attempts** the number of subjects in whom no device was passed into the working channel of the hysteroscope The primary reason for not passing a device is that the ostium of one or more fallopian tubes was not visualized
- **Bilateral placement rate** the proportion of subjects in whom bilateral placement was achieved amongst all study subjects in which at least one Essure device was passed into the working channel of the hysteroscope
- **Adjusted bilateral placement rate** the proportion of subjects in whom bilateral placement was achieved, excluding subjects in whom bilateral placement is, by definition, impossible Thus, excluded from this calculation are intentional unilateral placements (i e , it is known prior to the procedure that a subject lacks two anatomic fallopian tubes [unicornuate uterus] or a subject lacks intact tubes [e g , prior unilateral salpingectomy]) In ESS305 PAS, no such patients were enrolled

1.7. Statistical Approach

(b)(4)

1.8. Study History

Enrollment began in August 2007 and ended in March 2009 Study enrollment ceased after approval of P020014/S18, which showed that continued enrollment added little additional information for the main study questions As discussed in P020014/S18, the point estimate

(b)(4)

1.9. Excluded Subjects

A total of (b)(4) subjects were enrolled in ESS305 PAS However, the following were excluded

* See http //ftp sas com/techsup/download/stat/glmm800 sas and Littell RC, Milliken GA, Stroup WW et al 1996 SAS System for Mixed Models Cary, NC SAS Institute

- (b)(4)
-
-

Thus the study cohort consists of 587 subjects

2. Results

2.1. Non-Attempt Rate

Table 2 shows placement outcomes by physician and level of experience. A small number of physicians enrolled slightly more than 10 subjects, but in order to improve study estimate precision, these subjects were retained in the analysis (b)(4)

(b)(4)

* One subject had a vasovagal episode that resolved prior to discharge

Table 2 Placement outcomes by physician and level of experience

		Non-Attempt			
		No		Yes	
		Bilateral Placement			Total
		No	Yes		
Level of Experience	**MD Name**				
Experienced	(b)(4), (b)(6)				
Newly Trained					

* Note, in all tables in this report " " indicates no observations

	(b)(4), (b)(6)			
Total	16	565	6	587

2.1. Bilateral Placement Rate

Among (b)(4) subjects in whom at least one Essure device was passed through the hysteroscope, bilateral placement was achieved in 565 (b)(4) Bilateral placement rate by physician is shown in **Table 3** and **Table 4** (b)(4) of the physicians had (b)(4) placement rates (b)(4) (b)(4)

Table 3 Bilateral placement rate by physician and level of experience

Level of Experience			
Experienced		Newly Trained	
Physician	S/N (%)*	Physician	S/N (%)*
(b)(4), (b)(6)			
	Total	565/581 (97 2)	

S = successes N = number of subjects % = bilateral placement rate

Table 4 Counts of placement rates by physician

Bilateral Placement Rate (%)	Frequency
(b)(4)	

2.2. Non-Bilateral Placements

(b)(4)

Table 5 Reasons for non-bilateral placement in ESS305

Primary reason for placement failure	No of Subjects (% total)	Subject No
(b)(4), (b)(6)		

2.3. Bilateral Placement Rate by Level of Experience

(b)(4)

(b)(4)

2.4. Comparison to ESS205 Post-Approval Study

The first Essure post-approval study was a post-approval study of the ESS205 model of the Essure System. As noted in **Table 1**, the primary difference between the ESS205 and ESS305 devices is an improved mechanism for deployment and detachment of the micro-insert. In Conceptus' first post-approval study, the bilateral placement rate amongst subjects receiving the ESS205 device was (b)(4), the Essure System labeling was updated with this rate in P020014/S10. For this estimate, FDA requested that Conceptus

(b)(4)

Table 6 Comparison of current study to ESS205

Study	S/N (%)	Comment
ESS205	(b)(4)	
ESS305		

3. Summary

ESS305 PAS was a multicenter prospective study of the bilateral placement rate using the ESS305 delivery system. The study showed that

- The bilateral placement rate was very high (97.2%)
- The variation in placement rate across physicians was not more than expected due to random sampling
- The difference in bilateral placement rate across levels of physician experience was small (1.9%), statistically insignificant, and not clinically meaningful
- The bilateral placement rate was slightly better than that observed in ESS205
- The most common reason for non-bilateral placement was tubal spasm
- The non-attempt rate was very low (1%)

We drew the following conclusions

- Changes in the delivery system from ESS205 to ESS305 did not negatively impact the ability of physicians to place the device with a high rate of success
- The learning curve for Essure placement is extremely fast. After training and performing (b)(4) cases under proctorship, a newly trained physician has as high a bilateral placement rate as an experienced physician
- The major reason why Essure devices cannot be placed is anatomic in nature (tubal spasm) and not due to a deficiency in device or delivery system design

(b)(4)

P020014/R24/A2 C1

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NOV 24 2009

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Re: PMA P020014, Report #24, Amendment 2
Conceptus Essure® System for Permanent Birth Control

Dear Drs. Van Dole and Marinac-Dabic:

This amendment is to provide additional information in (b)(4)

(b)(4)

FDA Question:

(b)(4)

Table 1. Placement rates by study and physician group.

Study / Group	S/N (%)
ESS205 (newly trained physicians)	(b)(4)
ESS305 (newly trained physicians)	
ESS305 (experienced physicians)	

(b)(4)

(b)(4)

Table 2. Bilateral placement rate by physician and study among newly trained physicians.

Study	Physician Name	S/N	Study	Physician Name	S/N
ESS205 PAS	(b)(6)		ESS305 PAS	(b)(6)	

Please find three paper copies of the submission enclosed. 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 650.962.4078, by fax at 650.962.5194, or by email at rachelle.acuna-narvaez@conceptus.com. Thank you for your continued review of this report.

Warm regards,

Rachelle Acuña-Narvaez

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