P020014 | R32

Bayer HealthCare

FDA CDRH DMC
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March 19, 2014

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RE: ESSURE-NOVASURE Post-Approval Study
ESS-NSPAS/16975: 24-month Interim Report
PMA P020014/R032
Essure® System for Permanent Birth Control ESS305

To Whom It May Concern:

In accordance with 21 CFR 822, Bayer HealthCare is submitting three copies of the 24-month interim report on the Essure-NovaSure Post-Approval Study. Two copies are provided as e-copies and are the exact duplicate of the attached paper copy.

The information contained in this 24-month report on the Essure-NovaSure 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) 962-4147, by fax at (650) 691-4729, or by email at lorie.laird@bayer.com.

Sincerely,

Lorie Laird
Regulatory Affairs Associate

Post-Approval Study Status Report
24 Month Interim Report

A Study to Evaluate the Effectiveness of Essure Post-NovaSure Radiofrequency Endometrial Ablation Procedure Following a Successful Essure Confirmation Test

Essure-NovaSure PAS

Study# ESS-NSPAS

(Bayer Study #16975)

Date of Report: March 20, 2014

Data current to March 13, 2014

ESS-NSPAS/16975 – 24 Month Interim Report

1. GENERAL INFORMATION

1.1 Sponsor Information

Name: Bayer HealthCare LLC
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Establishment Registration Number: 2951250

Contact Person: Lorie Laird, Regulatory Affairs Associate
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1.2 Product Information

Product Name: Essure Permanent Birth Control System
Model Number: ESS305
Application Number: P020014 - S017
Supplement for Protocol Amendment: P020014 – S039

2. SUBMISSION INFORMATION

Date of Submission: March 20, 2014
Data included in this submission: Clinical Study Data
Date of Post-Approval Study Protocol and Supplement Approval: December 19, 2012

Type of Submission: *24-month Interim Report for Post-Approval Study to Evaluate the Effectiveness of Essure Post-NovaSure Radiofrequency Endometrial Ablation Procedure Following a Successful Essure Confirmation Test*

Additional Information: Supplement to change previously approved Post-Approval Study Protocol, Version 3 was submitted to FDA as P020014/S039, received by CDRH Document Control Center November 26, 2012; Approval for Version 3 was received on December 19, 2012.

3. STUDY INFORMATION

3.1 Study Purpose

3.1.1 Goals

This Post-Approval Study (PAS) is a prospective, multi-center, single-arm observational study to monitor and evaluate the effectiveness and safety of Essure when NovaSure Endometrial Ablation (EA) is performed following a successful Essure Confirmation Test (CT).

3.1.2 Objectives

- Evaluate the contraceptive failure rate of Essure when NovaSure is performed following a successful CT, and
- Monitor the incidence of adverse events and/or complications associated with the performance of NovaSure in the presence of Essure inserts.

3.1.3 Post-Approval Study Endpoints

- Occurrence of confirmed pregnancy at 1 and 3 years after NovaSure EA among subjects relying on Essure inserts for permanent birth control when NovaSure is performed following a successful Confirmation Test.
- Adverse event data.

3.2 Subject Population

The Post-Approval Study target population is subjects who have been identified as candidates for NovaSure Endometrial Ablation and have been relying on Essure inserts for permanent contraception (following a satisfactory CT). The target sample size is 220 women. (Eligibility criteria are provided in the study protocol.)

3.2.1 Subject Follow-up Schedule

Subjects will be followed for a total of three years post-NovaSure EA with evaluations to occur at the 1 week, 12 month, 24 month and 36 month follow-up time points.

3.3 Report Dates

The period covered by this report is from November 13, 2012 (date of first subject consent signed) through March 13, 2014.

3.4 Summary of Study Progress

3.4.1 Approval Dates

- Original Essure-NovaSure PAS FDA approval (protocol Version 2) - February 24, 2012.

- Central IRB, Ethical and Independent Review Services (E&I), Study Sponsor Approval (protocol Version 2) - May 1, 2012.
- PAS Supplement FDA approval (protocol Version 3) – December 19, 2012.
- Central IRB (E&I) Study Sponsor Approval (Version 3) (Bayer study #16975) - January 3, 2013.

3.4.2 Study Milestones

Table 1. *Revised Study Milestones*
(approved by FDA in last interactive review – Jan 2014)

Study start date – First subject enrolled (consent signed)	November 2012
Expected enrollment rate of subjects per month per site (currently there are 12 sites)	0.5
Expected rate per year of subjects enrolled	80
Expected date for subject enrollment completion	October 2015*
Expected date of final subject follow-up	November 2018
Expected date complete final PAS report	May 2019

*Assuming three more sites are added by June 2014.

3.4.3 Site Enrollment

Table 2. ***Current Site Enrollment***

Number of Sites Enrolling Subjects	Number of Sites with IRB Approval	Number of Sites Initiated	Number of Sites Closed*	Number of Sites to be Added
(b)(4)				

*Per investigator's request.

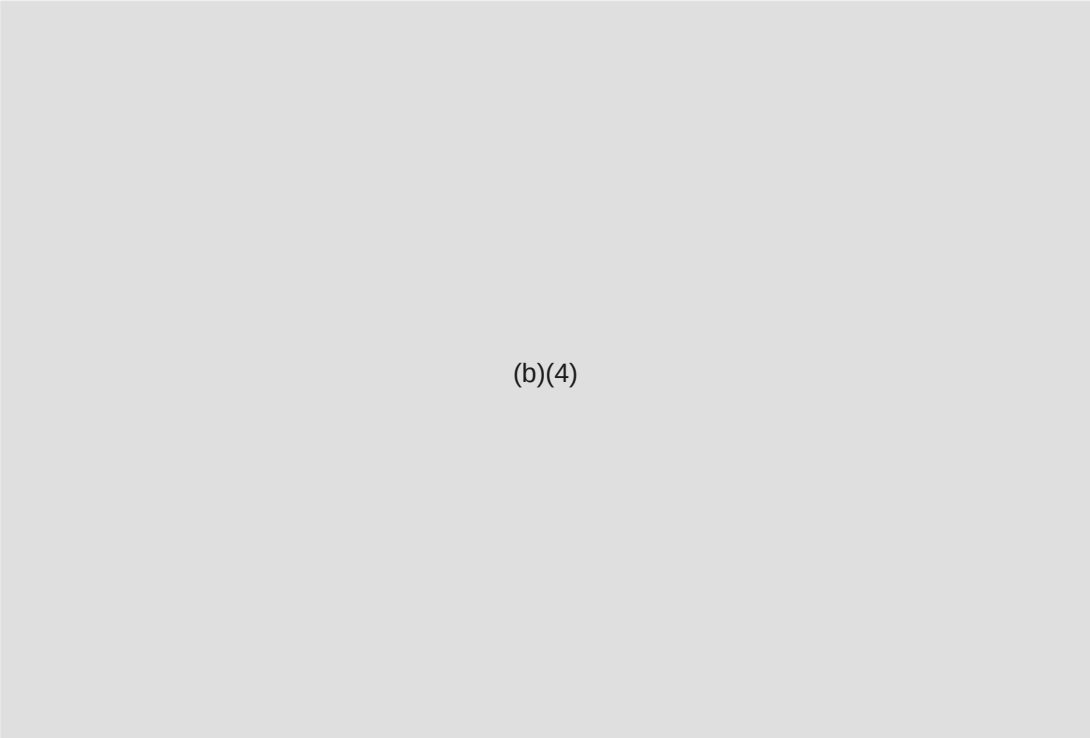
3.4.4 Subject Enrollment:

Subject Accrual Start Date (first subject consent signed): *November 13, 2012*
Subject Accrual Completion Date: *estimate October 2015*

3.4.5 Study Targets:

Table 3. *Number of Subjects and Percentage Having Reached Each Designated Study Visit (based on target sample size 220).*

NovaSure EA Procedure	One Week Post-EA Office Visit	One Year Post-EA Phone Call	Two Years Post-EA Phone Call	Three Years Post-EA Phone Call
(b)(4)				



The above graph shows the progression of study enrollment. As of the data cut off for this report, study enrollment is on target to meet the revised projected cumulative total that was presented and approved by FDA in the January 2014 interactive review.

3.5 Enrollment Improvement Strategies

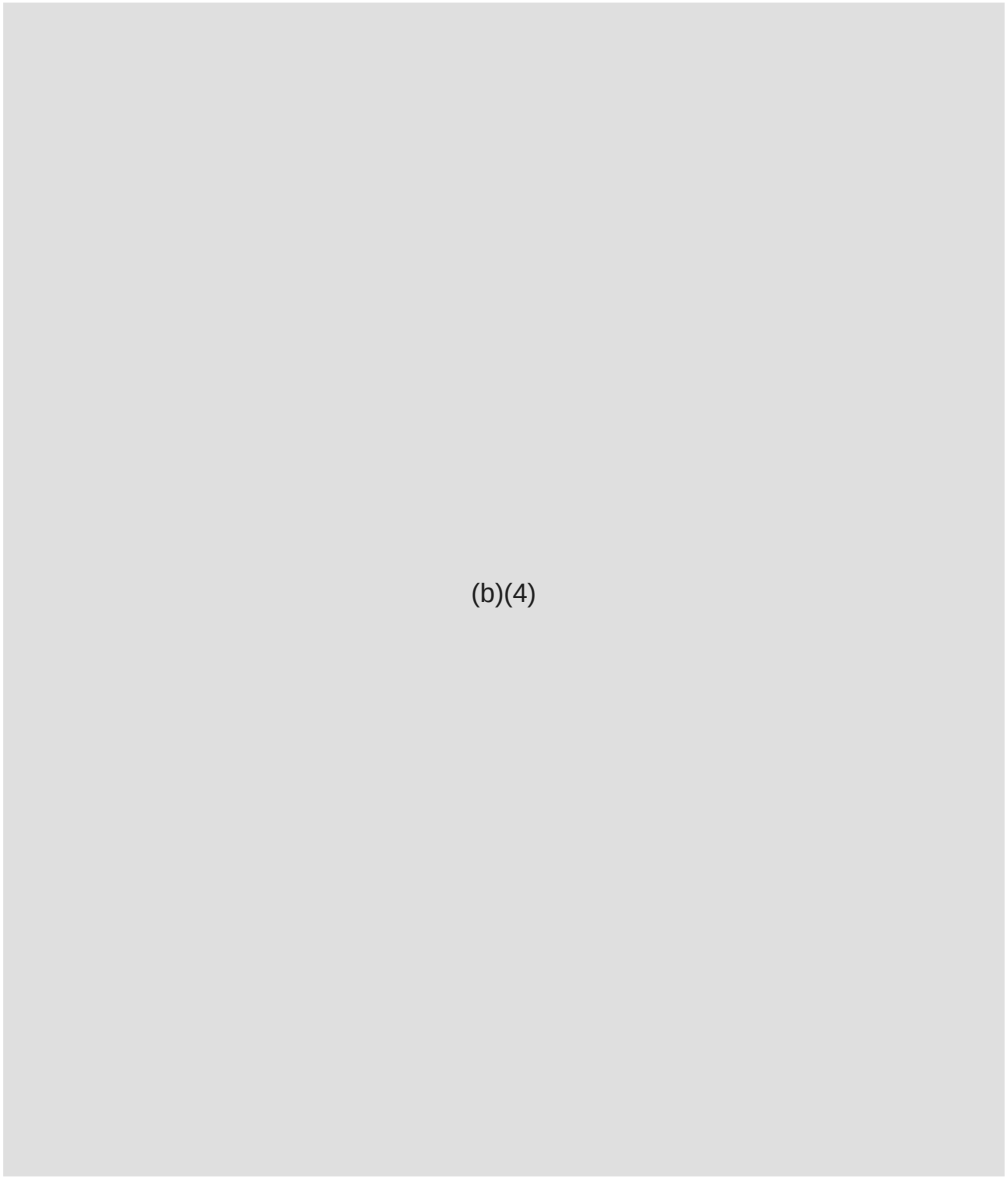
As noted in the 18-month report and interactive review in January 2014, the study team is working to ensure that target enrollment is met. Table 4 lists the current strategies to improve enrollment currently in place and their status at the time of this report.

Table 4. *Enrollment Improvement Strategies*

(b)(4)

3.6 Subject Tree & Subject Accountability

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


(b)(4)

3.7 Subject Demographics

Demographic characteristics of the 68 enrolled subjects are presented below.

Table 5. *Age of Enrolled Study Subjects* (b)(4)

<28 years old	28-33 years old	≥ 34 years old
(b)(4)		

Table 6. *Demographics of Enrolled Study Subjects* (b)(4)

Race	Number
American Indian or Alaska Native	(b)(4)
Asian	
Black or African American	
Native Hawaiian or Other Pacific Islander	
White	
Other	0
Ethnicity	**Number**
Hispanic	(b)(4)
Not Hispanic	
Other	**Mean**
Gravidity (range 0-5)	(b)(4)
Parity (range 0-4)	
BMI (range19-42)	

3.8 Summary of Safety and Effectiveness Data

3.8.1 Effectiveness Data

Occurrence of confirmed pregnancy at 1 year and 3 years among subjects relying on Essure inserts for permanent birth control when NovaSure is performed following a successful Essure Confirmation Test. At this time, no pregnancies or expulsions have been reported.

3.8.2 Adverse Event Data

Unanticipated Device Effects: None
Adverse Events: 14

Table 7 summarizes the adverse events that have occurred during the study, the start and stop date, severity, relatedness assessment and outcome. None of the adverse events are serious. Days from Novasure procedure 0 indicates that the AE start date was the same day as the NovaSure EA procedure.

Table 7. *Adverse Events*

aerpt	ID	AE ID	AE Verbatim	Days from Nova-sure to AE	Time Frame	AE Start Date	AE Stop Date	Severity	Relatedness to Es-sure Device	Relatedness to No-vasure Device	Relatedness to No-vasure Proce-dure	Relatedness to Pre-existing Condi-tion	Outcome
1	013009		.		NA	.	.	Not checked	Not checked	Not checked	Not checked	Not checked	NA
2	001002		pelvic cramping	0	Day 0	11/27/12	11/28/12	Mild	Not related	Not related	Definitely	Not related	Recovered w/o treatment
3	007006		Pt had nausea following Novasure procedure	0	Day 0	11/07/13	11/07/13	Severe	Not related	Not related	Probably	Not related	Recovered w/ treatment
4	007006		Pt had severe pelvic pain following Novasure procedure	0	Day 0	11/07/13	11/07/13	Severe	Not related	Not related	Probably	Not related	Recovered w/ treatment
5	001025		pelvic pain	1	1-7 days	02/12/14	03/01/14	Moderate	Not related	Unlikely	Possibly	N/A	Recovered w/ treatment
6	001017		pelvic pain	5	1-7 days	11/03/13	11/05/13	Mild	Not related	Not related	Possibly	Unlikely	Recovered w/o treatment
7	005003	(b)(4)	Vaginal Itching	8	8-365 days	12/17/13	01/08/14	Mild	Not related	Not related	Possibly	Not related	Recovered w/o treatment
8	007002		fever,pain	10	8-365 days	09/08/13	10/01/13	Mild	Not related	Not related	Probably	Not related	Undetermined
9	007002		infection following ablation	10	8-365 days	09/08/13	10/01/13	Mild	Not related	Not related	Probably	Not related	Recovered w/ treatment
10	001001		longer crampier periods	18	8-365 days	12/01/12	12/03/13	Moderate	Not related	Unlikely	Probably	Not related	Recovered w/ treatment
11	001004		dysmenorrhea	29	8-365 days	01/18/13	01/19/13	Mild	Not related	Not related	Possibly	N/A	Undetermined
12	011001		Tenderness at surgery site from 8/8/13 procedure	77	8-365 days	08/08/13	12/05/13	Mild	Not related	Not related	Not related	Not related	Undetermined
13	011001		Patient had Urinary tract infection	96	8-365 days	08/27/13	09/26/13	Mild	Not related	Not related	Not related	Not related	Recovered w/ treatment
14	001009		postcoital bleeding	145	8-365 days	12/01/13	.	Mild	Not related	Unlikely	Possibly	Unlikely	Undetermined

3.8.3 Protocol Deviations

There have been approximatel (b)(4) otocol deviations to date. They have been classified into four categories with frequency of occurrence shown for each. The second category covers a deviation that occurred at many of the sites that routinely performed a biopsy prior to endometrial ablation to rule out preexisting endometrial pathology. This deviation has been previously waived by the sponsor, but is still being reported as a study deviation. This additional procedure prior to NovaSure will be incorporated into the next amendment of the study protocol.

Table 8. *Protocol Deviations*

Deviation Category	Quantity
Informed consent not properly obtained/ Study procedure performed prior to consent	(b)(4)
Subject had intrauterine procedures at the time of NovaSure EA	
Follow-up visit out of window / Required study evaluation/ procedure not performed/ or done out-of-window	
Other deviations (mostly due to undergoing Essure CT less than 90 days after Essure procedure).	