(b) (6)
U.S. Food and Drug Administration
Center for Devices and Radiological Health
(b) (6)
10903 New Hampshire Ave.
WO66-3211

January 04, 2018

Bayer HealthCare
Pharmaceuticals Inc.
100 Bayer Boulevard
P.O. Box 0915
Whippany, NJ 07981-0915
Phone: (b) (6)
Fax: (b) (6)

**RE**: **Postmarket Surveillance (PS) Study: PS160001/R002/A001**
**12-Month Interim Postmarket Surveillance Report Amendment**
Trade Name: Essure System for Permanent Birth Control
Reference PMA: P020014

Dear (b) (6) :

Reference is made to the teleconference between FDA and Bayer on December 11,

2017 and the request to amend information in Bayer's 12 month interim report for PS160001 study. Reference is also made to FDA's approval of the Essure 522 study plan on September 2, 2016.

Bayer is herewith submitting the 12-month Interim Postmarket Surveillance Report with updated information, specifically the subject accrual completion date, the Bayer Regulatory contact information and one new paragraph at the end of section3.4.2 (see **Attachment 1**).

The information contained in this submission is considered confidential, and Bayer therefore requests protection of this information in accordance with 18 USC 1905, 21 USC 331 (1), 5 USC 522.

This submission is provided in accordance with the eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff (October 10, 2013).

Bayer HealthCare Pharmaceuticals certifies that this submission has been scanned for viruses and is virus free using TREND MICRO™ Office Scan™ , Program Version Office Scan™, Program Version 10.6 or higher. For any questions regarding eCopy technical aspects of this electronic submission, please contact (b) (6) or by email at (b) (6)

Bayer looks forward to closely working with the FDA on this post market surveillance study. Should you require additional information, please feel free to contact (b) (6) .

(b) (6)

## ATTACHMENT 1: 12-Month Interim Postmarket Surveillance Report

cc: (b) (6)

# 12-Month Interim Postmarket Surveillance Report

An open-label, non-randomized, prospective observational cohort study to assess post-procedural outcomes in two cohorts of women who chose to undergo either hysteroscopic sterilization (Essure®) or laparoscopic tubal sterilization

Bayer Study (b) (4)

Postmarket Surveillance
Application #PS160001

Date of Report: 02 SEP 2017

Data Current to:

30 JUN 2017 (data extract)

09 AUG 2017 (site/subject recruitment metrics)

# Table of Contents

## Table of Tables



## List of abbreviations

| | |
|---|---|
| AE | Adverse event |
| FAS | Full analysis set |
| GI | Gastrointestinal |
| IRB | Institutional review board |
| LTS | Laparoscopic tubal sterilization |
| MedDRA | Medical Dictionary for Medical Activities |
| (b)(4) | |
| PSV | Pre-selection visit |
| SAE | Serious adverse event |
| SOC | System organ class |
| TEAE | Treatment-emergent adverse event |

# 1. General Information

Postmarket Surveillance Application Number: PS160001

## 1.1 Sponsor Information

Name: Bayer Healthcare LLC

Address: 100 Bayer Blvd.
P.O. Box 915
Whippany, NJ 07981 USA

Contact Person: (b) (6)
(b) (6)
Telephone: (b) (6)

Email Address: (b) (6)

## 1.2 Product Information

Device trade name and model number: Essure® System (ESS305)

Date of the 522 order: 29 FEB 2016

Date of postmarket surveillance plan approval: 02 SEP 2016

# 2. Report Information

Date of report: 02 SEP 2017

Data included in this report: clinical study

Type of submission: interim Postmarket Surveillance Report

# 3. Postmarket Surveillance Information

## 3.1 Study Purpose

### 3.1.1 Goals

Study (b) (4) is an open-label, non-randomized, continuous enrollment, prospective observational, postmarket surveillance study of 2 cohorts of subjects who chose to undergo:

- hysteroscopic sterilization (Essure System), or
- laparoscopic tubal sterilization.

### 3.1.2 Objectives

(b) (4)

### 3.1.3 Study Endpoints

(b) (4)

(b) (4)

## 3.2 Study Population

The planned study population includes subjects of reproductive age, between 21 and 45 years of age, who have not been pregnant within the past 6 weeks.

The Essure study population group will include subjects who chose to undergo hysteroscopic sterilization and who meet the criteria as outlined in the most current approved version of the Essure Instructions for Use.

(b) (4)

A sample size of 1400 subjects in each treatment group is planned.

Subjects will be followed for a total of 36 months post-procedure. Table 1 provides the subject follow-up visit schedule.

**Table 1 Subject Follow-up Visit Schedule**

| Time of Visit | Office Visit | Telephone Contact |
|---|---|---|
| (b) (4) | | |

## 3.3 Report Dates

The postmarket surveillance plan was approved by the Food and Drug Administration on 02 SEP 2016. The milestone information regarding site and subject recruitment efforts presented in Section 3.4 is current through 09 AUG 2017.

The data extract used for the tabulations provided in Section 3.5 to Section 3.8 of this report includes all data entered into the database as of 30 JUN 2017. Subjects enrolled between 30 JUN 2017 and 09 AUG 2017 are not included in these tabulations. Data are preliminary and will be updated with ongoing monitoring efforts.

The anticipated study/surveillance completion date is MAY 2023.

## 3.4 Summary of Study/Surveillance Progress Milestones/Timeline Elements

### 3.4.1 Site Recruitment Status

A total of 75 sites is planned. The expected completion date for site enrollment is May 2018. The site enrollment progress as of 09 AUG 2017 is shown below. Based on the progress made since the 02 MAR 2017 6-month surveillance report, the study is on target to achieve the MAY 2018 target date for full site enrollment.

- number of sites contacted: approximately 2531
- number completing Questionnaire #1 (Interest): 182 (140: Yes; 18: Maybe; 24: No)
- number completing Questionnaire #2 (Feasibility): 143
- number identified for pre-selection visit (PSV): 98
- number of PSVs completed: 81
- number of sites approved for participation: 69
- number of IRB approvals: 40
- number of clinical sites activated (approved to begin screening): 34
    - type of facilities:

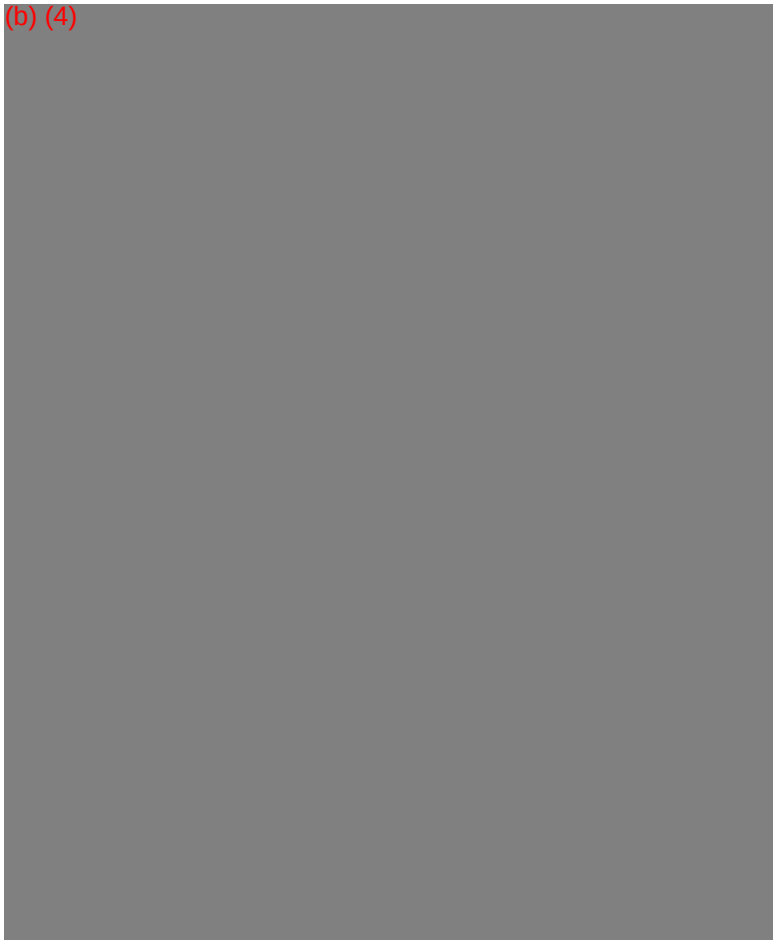
- University Hospital: 3
- Public/Private Hospital: 0
- Research Center: 31

A summary of subject enrollment by study site is shown in Table 2.

**Table 2 Subject Enrollment by Study Site**

| Site # | Essure | LTS | Total |
|---|---|---|---|
| (b) (4) | | | |

(b) (4)



### 3.4.2 Subject Recruitment and Accounting

A total enrollment of 2800 subjects (1400 subjects in each group) is planned. A subject is considered to be enrolled after signing informed consent. The milestones summarized below are based on data current through 09 AUG 2017. Additional data regarding disposition, baseline characteristics, and safety results for the cohort of subjects enrolled as of the 30 JUN 2017 extract date are summarized in Section 3.5 to Section 3.8.

- number of subjects enrolled (signed informed consent): 55
- subject accrual start date: 03 MAY 2017
- number of sites with subjects enrolled: 13
- subject accrual completion date: target = MAY 2020
- percentage of subjects reaching each designated study phase: see Table 3
- comparison of target versus actual enrollment and follow-up: first subject enrolled was achieved 3 weeks prior to the target date of 29 MAY 2017 and subsequent subject enrollment is on track with target projections

- the rate of enrollment is expected to vary throughout the life of the study, with the planned enrollment period requiring approximately 78 subjects/month on average with 75 sites recruiting. It is too early to assess performance against this measure but enrollment progress will be closely monitored for potential impact to timelines as the study continues.

**Table 3 Subject Accountability by Treatment Group (As of 09 AUG 2017)**

| Milestone | Essure | Laparoscopic Tubal Sterilization |
|---|---|---|
| Enrolled (signed informed consent) | 30 | 25 |
| Screen-failed | (b) (4) | |
| Screened but no procedure yet | | |
| Had procedure visit | | |
| Procedure | | |
| Attempted | | |
| Not attempted[a] | | |
| Told to rely | | |
| Had 1-week telephone contact | | |
| Had 3-month telephone contact | | |
| Discontinued[a] | | |
| Lost to follow-up | | |

(b) (4)

## 3.5 Subject Disposition

The disposition of subjects enrolled as of the 30 JUN 2017 data extract is shown in Table 4. Of the (b)(4) subjects in the Essure group and (b)(4) subjects in the LTS group who signed

informed consent and entered the screening phase, (b)(4) and (b)(4) subjects, respectively, had a procedure visit and had the procedure attempted as of 30 JUN 2017. (b) (4) subjects were screen-failed and (b) (4) subjects were discontinued from the study. (b) (4) subjects in the Essure group had reached their 3-month confirmation test time point as of the data extract date.

## Table 4 Disposition – Overview (All Enrolled Subjects) (As of 30 JUN 2017)

| Disposition | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| Number (%) of subjects enrolled | (b) (4) | | |
| Screening Failures | | | |
| Entered Procedure Phase | | | |
| No Procedure Attempted | | | |
| Procedure Attempted | | | |
| Told to Rely | | | |
| Completed the End of Study visit | | | |
| Discontinued from the Study | | | |

(b) (4)

## 3.6 Subject Demographics and Baseline Characteristics

(b) (4)

**Table 5 Demographic Characteristics (Full Analysis Set)**

| | Essure (b) (4) | Laparoscopic Tubal Sterilization (b) (4) | Total (b) (4) |
|---|---|---|---|
| (b)(4) | | | |

Source: Section 5.1

## 3.7 Procedure-Related Findings

(b)(4)

## 3.8 Interim Safety Findings

(b)(4)

**Table 6 Overall Summary of Adverse Events (Full Analysis Set)**

| | Essure (b) (4) | | Laparoscopic Tubal Sterilization (b) (4) | | Total (b) (4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 6 Overall Summary of Adverse Events (Full Analysis Set) (continued)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4)) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 6 Overall Summary of Adverse Events (Full Analysis Set) (continued)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 7 Subject Incidence of Treatment-emergent Adverse Events (TEAEs) by SOC and Preferred Term (Full Analysis Set)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

## 4. Summary

Study activities related to site and subject recruitment are on track to achieve full site enrollment by MAY 2018 and subject enrollment by MAY 2020. As of the data extract date (30 JUN 2017), (b)(4) ESSURE and (b)(4) LTS procedures had been performed. (b)(4)
(b)(4)

# 5. Appendix

## 5.1 Demographics and Baseline Characteristics (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Demographics and Baseline Characteristics (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Demographics and Baseline Characteristics (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | | |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

(b)(4)

## Demographics and Baseline Characteristics (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## 5.2 Summary of Reproductive and Menstrual History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## 5.3 Summary of Contraceptive Method at Baseline (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## 5.4 Summary of Abdominal/Pelvic Surgical History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Summary of Abdominal/Pelvic Surgical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Summary of Abdominal/Pelvic Surgical History (Full Analysis Set) (continued

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## 5.5 Medical History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | [redacted] | [redacted] | [redacted] |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## 5.6 Prior Medication (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |
| | (b) (4) | | |

(b) (6)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

(b) (4)

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

| | | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|---|
| (b) (4) | | (b) (4) | (b) (4) | (b) (4) |
| (b) (4) | | | | |

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

(b) (4)

## Prior Medication (Full Analysis Set) (continued)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b) (4) | | | |

(b) (4)

## 5.7 Adverse Events – Subject Listing (Full Analysis Set)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

**MEMORANDUM**

Date: October 26, 2017 (amended January 24, 2018)

From: (b) (6)

Subject: PS160001/R002 and PS160001/R002/A001
Essure System for Permanent Birth Control, Bayer Pharma AG
522 Study Requirement Name: Postmarket Surveillance Study
Epidemiologic Review of Postmarket Surveillance (PS) Study Interim Report

PS Order: Date of PS Order: February 29, 2016
ODE/OIR Document(s) on which the PS order was issued: P020014

To: (b) (6)

Through: (b) (6)

| Conclusion/Recommendation: |
| --- |
| After interactive review, no deficiencies remain. The interim report (PS160001/R002) can be accepted. |
| 522 Requirement Progress Status: Progress Adequate |

## Purpose:

The purpose of this memorandum is to present the epidemiologic review for the 12-month 522 Postmarket Surveillance (PS) Study Interim Report for the Essure System for Permanent Birth Control submitted by Bayer Pharma AG.

This memo includes:

- background information
- PS study protocol overview
- the review and assessment of the interim study results
- PS study tracking information

- overall conclusions and recommendations
- any applicable deficiencies.

# Background:

## Device Description

A. Essure System Components

The Essure System is comprised of the Essure micro-insert, a disposable delivery system, and a disposable split introducer.

Essure Micro-Insert

The Essure micro-insert is a spring-like device that consists of a stainless steel inner coil, a nickel titanium (Nitinol) expanding outer coil, and polyethelene terephthalate (PET) fibers. The PET fibers are wound in and around the inner coil. The micro-insert is 4 cm in length and 0.8mm in diameter in its wound down configuration. When released from the delivery system, the outer coil expands to 1.5 to 2.0 mm in diameter to anchor the micro-insert in the varied diameters and shapes of the fallopian tube. The spring-like device is intended to provide the necessary anchoring forces during the acute phase of device implantation (3 months post-micro-insert placement), during which time the PET fibers are eliciting tissue in-growth into the coils of the Essure micro-insert and around the PET fibers.

The Essure Micro-insert is provided attached to the delivery wire, in a wound-down configuration. The delivery wire is composed of a nitinol core wire, which is ground at the distal end to result in a flexible, tapered profile. The device is constrained by the release catheter, which is sheathed by a flexible delivery catheter. A black positioning marker on the delivery catheter aids in proper placement of the device in the fallopian tube.

The delivery handle controls the device delivery and release mechanism. The thumbwheel on the delivery handle retracts both the delivery catheter and the release catheter. The button allows the physician to change the function of the thumbwheel from retracting the delivery catheter to retracting the release catheter. The delivery wire is detached from the micro-insert by rotating the system.

Split Introducer

The split introducer is placed into the sealing cap of the working channel of the hysteroscope, and is intended to help protect the Essure Micro-insert as it is being passed through the sealing cap of the hysteroscope working channel.

B. Mechanism of Action

1. Placement at Utero-Tubal Junction (UTJ)

The Essure Micro-insert is intended for placement into the fallopian tube with the implant portion of the device spanning the utero-tubal junction (UTJ). For purposes of micro-insert placement, the UTJ is

defined as the portion of the fallopian tube, just as it enters the uterus. Placement at the UTJ is expected to aid in anchoring since it most consistently represents the narrowest portion of the fallopian tube. Expulsion of the Essure Micro-insert has occurred when micro-insert placement was too proximal. If the device is placed without any trailing portion of the device in the uterus, then direct visualization of device location is not possible.

2. Tissue In-Growth

The effectiveness of the Essure Micro-insert in preventing pregnancy is believed to be due to a combination of the space-filling design of the device and a local, occlusive, benign tissue response to the PET fibers. The tissue response is the result of a chronic inflammatory and fibrotic response to the PET fibers. It is believed that the tissue ingrowth into the device caused by the PET fibers results in both device retention and pregnancy prevention.

3. Permanency of Tubal Occlusion (and Sterilization)

The long-term nature of the tissue response to the Essure micro-insert is not known. The majority of the clinical data regarding PET in the fallopian tube is based on 12-24 months of implantation, with little data at 36 months. Therefore, beyond 24 months, the nature of the cellular fibrotic response and the ability of the response and the device to maintain occlusion are not known.

**Indications for Use**

The Essure System is indicated for women who desire permanent birth control (female sterilization) by bilateral occlusion of the fallopian tubes.

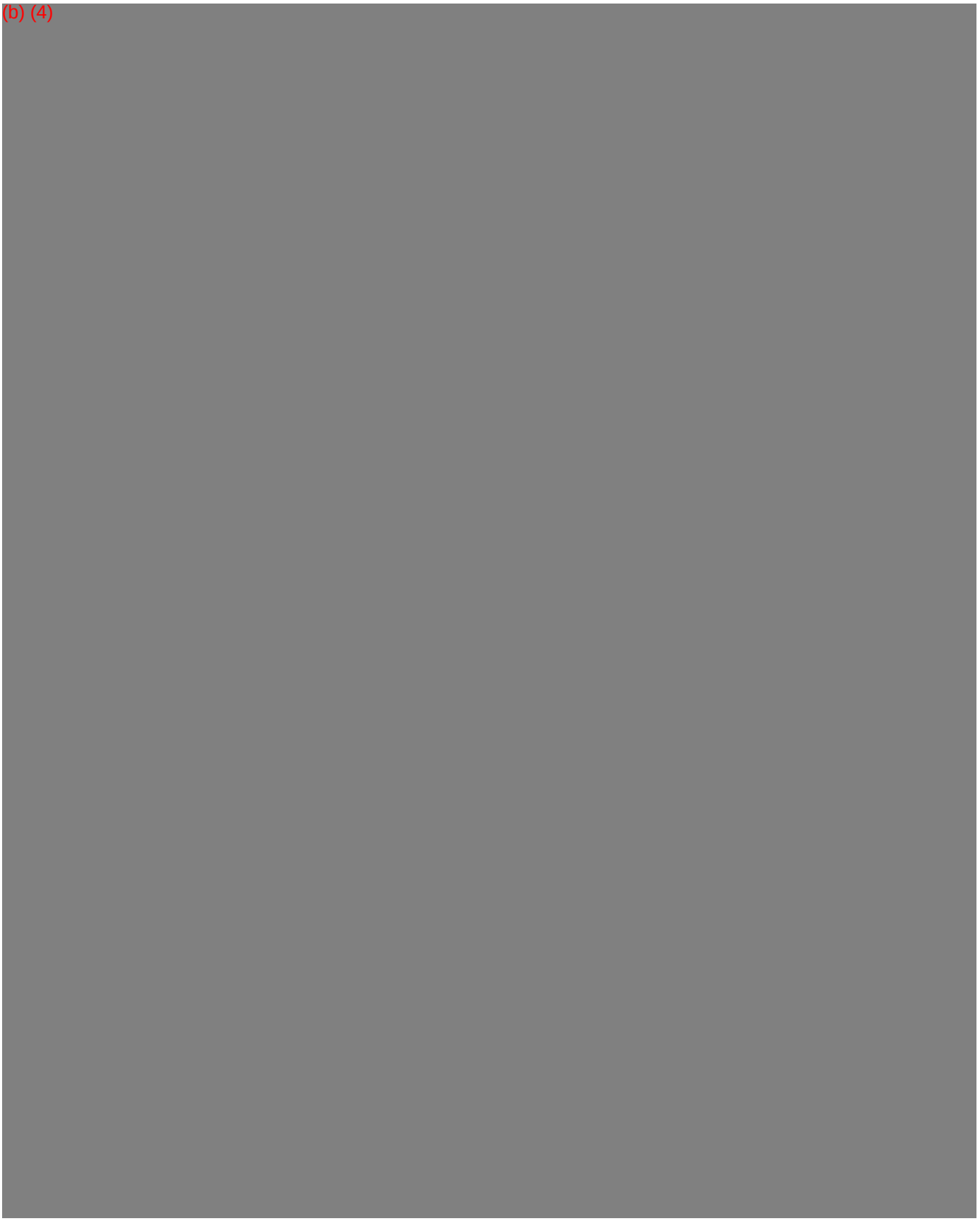
**PS Order**

On September 24, 2015, FDA convened a meeting of the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee (see transcript), and the panel recommended additional data collection via postmarket surveillance. On February 29, 2016, FDA issued a 522 order for the Essure Permanent Birth Control System.

## PS Study Protocol Overview:

(b) (4)

(b) (4)



| Study Element | Description |
|---|---|
| **Real-World Evidence (RWE)** | N/A |
| **Study Design** | Open-label, non-randomized, prospective observational cohort study of two cohorts of subjects who chose to undergo either hysteroscopic sterilization (Essure) or laparoscopic tubal sterilization. |
| **Study Hypothesis** | There is no hypothesis testing. |
| **Study Population** | The study population will include subjects of reproductive age, between 21 and 45 years of age who have not been pregnant within the past 6 weeks. The study population will include women who chose to undergo hysteroscopic sterilization (Essure) and who meet the criteria as outlined in the Essure Instructions for Use (IFU).<br><br>Women seeking laparoscopic tubal sterilization must be considered appropriate surgical candidates by the investigator. |
| **Sample Size** | 2,800 women (1,400 per arm) enrolled at 50-75 sites.<br>(b)(4) [redacted] |
| **Study Endpoints** | Follow-up measures will include adverse event assessment, medical history including gynecological procedures, patient reported outcome (PRO) measures for chronic pelvic pain and abnormal uterine bleeding, bloodwork for women with certain adverse events, and analysis of removed Essure devices.<br><br>Key Endpoints:<br>Pain: The proportion of subjects reporting AEs of chronic lower abdominal and/or pelvic pain after insertion of Essure System (ESS305)<br>(b)(4) [redacted]<br><br>Bleeding: The proportion of subjects reporting AEs of abnormal uterine bleeding after insertion of Essure System (b)(4) [redacted] (b)(4) [redacted] (b)(4) [redacted]. Total incidence of new onset or worsening abnormal bleeding events will be based on AE reporting.<br><br>Hypersensitivity/allergy/autoimmune disorders: The proportion of subjects with adjudicated new onset (b)(4) [redacted] allergic/hypersensitivity reactions (b)(4) [redacted] |

| Study Element | Description |
|---|---|
| | (b)(4) [redacted]<br><br>Proportion of subjects undergoing invasive gynecologic surgery (b)(4) [redacted]; including Essure insert removal (b)(4) [redacted]<br><br>Additional endpoints:<br>• Patient reported outcome measures (b) (4) [redacted]<br>• Rates of AEs |
| **Length of Follow-up and Frequency of Follow-up Assessments** | (b)(4) [redacted] 36 months. |
| **Enrollment Plan and Follow-up Measures** | (b)(4) [redacted] |
| **Statistical Plan** | (b) (4) [redacted] |

| Study Element | Description |
|---|---|
| | (b) (4) |

*Timeline for Study Implementation (approved on September 2, 2016: PS160001/A002)*

| Milestone: | Date: |
|---|---|
| Expected date of study initiation | September 2016 |
| Expected monthly number of study sites with IRB approvals | Approximately 8 sites/month |
| Expected date of initiation of subject enrollment | May 2017 |
| Expected number of subjects enrolled per month | Approximately 78 patients/month (when all sites activated) |
| Expected date of enrollment completion | May 2020 |
| Expected date of study follow-up completion | May 2023 |
| Expected date for final report submission | September 2023 |

## PS Study Interim Status/Results and Assessments:

Number of IRB Approvals, Sites and Study Participants

| Study Elements |
|---|
| **Number of IRB Approvals** |
| Description |
| ▪ 40/50 (80%) |
| Assessment |
| ▪ **Acceptable.** |
| **Number of study sites enrolled** |
| Description |
| ▪ 34/50 (68%) |
| Assessment |

- Site enrollment is expected to be completed in May 2018. The sponsor reported 34 sites enrolled as of August 9, 2017, which represents an increase of 31 sites since May 3, 2017. In the interactive review response (Attachment 1), the sponsor reported that this had increased further to 44 sites as of October 19, 2017. The study has made acceptable progress toward site enrollment. **Progress adequate**.
- The 522 study is intended to collect surveillance data that is representative of the patient population, with multiple types of study sites. The submission stated that 31 of 34 sites were classified as "research centers"; however, it was unclear what types of sites were included in this classification. It is important to ensure that procedures taking place as part of routine clinical practice (i.e., at private medical practices) are represented in the study, to minimize potential bias. Therefore, interactive review was initiated in order to clarify the type of sites that have been enrolled to date. The sponsor's response is in Attachment 1. The sponsor provided more specific information about the enrolled sites, which shows that any center participating in research could be considered a "research center", and therefore this classification includes private practices and public/private/university hospitals. According to the update on October 19, 2017, twenty-three (23) of the 44 sites are private practice. The response is **acceptable** and the concern is resolved.

**Number of subjects enrolled**

Description

- 55/2400 (2.3%)
- (b)(4)
- (b)(4)

Assessment

- 55 patients have been enrolled as of August 9, 2017, which represents an increase of 54 patients since May 3, 2017. Interactive review was initiated to request an enrollment update (see Attachment 1); the sponsor reported that 136 (5.7%) patients have been enrolled as of October 19, 2017. The study enrollment is progressing. **Progress Adequate**.
- (b)(4)

**Follow-up rate**

Description

- (b)(4)
-

Assessment

(b) (4)

***AMENDMENT (JANUARY 24, 2018):*** **After the decision letter for PS160001/R002 was issued on October 26, 2017, the two following issues were identified with the report and study timeline:**

- **The milestones in the 12-month report (R002) do not match the accepted study timeline with regards to the goal for patient enrollment completion; report states October 2020, and timeline states May 2020. An amended report needs to be submitted.**
- (b) (4) [redacted]

**Therefore, a teleconference was held with the sponsor on December 11, 2017 (see Attachment 2 for meeting minutes). The sponsor agreed to submit an amended report to correct the goal for patient enrollment completion. The amended report (PS160001/R002/A001) was received at FDA on January 4, 2018. On page 12/65 of the submission, the target date for subject accrual completion has been revised to May 2020, which is consistent with the accepted study timeline.The sponsor also provided updated regulatory contact information and one new paragraph (Section 3.4.2, page 13/65) which states the following:**

> ***"…the rate of enrollment is expected to vary throughout the life of the study, with the planned enrollment period requiring approximately 78 subjects/month on average with 75 sites recruiting. It is too early to assess performance against this measure but enrollment progress will be closely monitored for potential impact to timelines as the study continues."***

(b)(4) [redacted]

**Summary of Interim Study Results for the 522 Webpage**

| Study Elements | Description |
|---|---|
| Number of study sites enrolled | As of October 19, 2017, 44 study sites have been enrolled. |
| Number of subjects enrolled | As of October 19, 2017, 136 patients have been enrolled. |

## PS Study Tracking Information:

1. What is the Overall Study Status? Check only one.

| | | |
|---|---|---|
| | Plan Pending | FDA has not approved the study protocol, and it has been less than 6 months since issuance of the order. |
| | Plan Overdue | FDA has not approved the study protocol, and it has been 6 months or more since issuance of the order. |
| | Study Pending | The protocol has been approved, but no subjects have been enrolled. |
| X | Progress Adequate | The study has begun, and the study progress is consistent with the protocol (e.g., meeting enrollment schedule, follow-up rates, endpoints evaluated). |
| | Progress Inadequate | The study has begun, but the study progress is inconsistent with the protocol (e.g., not meeting enrollment schedule, missing timepoint evaluations, poor follow-up rates, not all endpoints evaluated). |
| | Completed | The sponsor has fulfilled the condition of approval, and FDA has closed the study. This is a final study status. |
| | Terminated | The sponsor has not fulfilled or cannot fulfill the condition of approval (e.g., study questions are no longer relevant, sponsor withdraws PMA, data cannot answer 522 question), and, after all appropriate efforts to fulfill the condition of approval have been exhausted, FDA has terminated the study. This is a final study status. |
| | Other | Used when the study status does not fit another category (e.g., not marketing the device and have no plans to market the device, change in ownership underway, redesigning device and need PMA approval prior to use in a PAS, pending separate study being used to address condition of approval). This is an interim study status. |

## Deficiency List:

None

### Advisory

1. Please be advised that your study status will be marked as "Progress Adequate" on the Section 522 Postmarket Surveillance Studies webpage (www.fda.gov/522studies).

(b) (6)

cc: (b) (6)

Document History:

| Date | Activity | Initials |
|---|---|---|
| 10/25/17 | Drafted | (b) (6) |
| 10/25/17 | Reviewed/Cleared | |
| 10/26/17 | Finalized | |
| 1/23/18 | Amended (pages 10, 16) | |
| 1/23/18 | Reviewed/Cleared | |
| 1/23/18 | Finalized | |

| | |
|---|---|
| Reviewer's Sign-Off | (b) (6) |
| Branch Chief Sign-Off | |

Attachment List

Attachment 1: Interactive Review Response

Attachment 2: Meeting Minutes (December 11, 2017)

## Attachment 1: Interactive Review Response

**From:** (b) (6)
**To:**
**Cc:**
**Subject:** RE: PS160001/R002 Interactive Review Request (reply requested by 10/19)
**Date:** Thursday, October 19, 2017 7:19:10 PM
**Attachments:** image009.png
image001.png
Bayer POET 18894_Selected Sites 18Oct2017.xlsx

---

Dear (b) (6)

Thank you for the email and questions regarding the study. Please see the response to your queries below.

Enrollment has increased since the report data cut-off, and progress towards site identification and activation remains ongoing. Please find an update to the reported figures below:

- number of subjects enrolled (signed informed consent): 136
- number of sites approved for participation: 71
- number of IRB approvals: 50
- number of clinical sites activated (approved to begin screening): 44
    - type of facilities:
        - University Hospital: 3
        - Public/Private Hospital: 3
        - Research Center: 3
        - Private Practice: 23
        - Private Practice/Research Center: 8
        - Public/Private Hospital/Private Practice/Research Center : 2
        - Public/Private Hospital/University Hospital: 1
        - University Hospital/Research Center: 1

As to facility types, shared here are the verbatim responses the sites reported on our Feasibility Questionnaire, which better conveys their designation. As any center participating in research could be classified as a "research center", and this designation could be more informative, we will in subsequent reports provide the verbatim responses as done here.

Additionally, please find attached a tracker showing all selected sites (not just those open to enrollment) with their self-identified facility type and city/state so you can see the distribution for the study overall. For site status, active is all sites that are approved to begin screening, planned is all sites that are approved for participation but not yet active, and declined is all sites that were approved for participation but have since opted not to participate.

Please feel free to contact me if you have additional questions.

Thank you

(b) (6)

**From:** (b) (6)
**Sent:** Tuesday, October 17, 2017 11:39 AM
**To:** (b) (6)
**Cc:**
**Subject:** PS160001/R002 Interactive Review Request (reply requested by 10/19)

Good afternoon,

I am reviewing the 12-month interim report for PS160001, and I would like to initiate interactive review with you. In the submission, you state that as of August 9th, there were 55 patients enrolled, 69 sites approved for participation, 40 IRB approvals, and 34 sites activated. As referenced in Section 11 of the study protocol, FDA plans to update the 522 website (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm?t_id=356&c_id=3854) with site and patient enrollment numbers after each interim report. It is anticipated that enrollment may have increased since the August 9th data extract date in the report. Therefore, please send an update regarding current patient and site enrollment.

In addition, the submission states that 31 of the 34 currently activated sites are categorized as research centers. However, it is not clear what types of sites are included in the category of research center (b)(4)
(b)(4)
(b)(4) Please provide a list of the currently activated sites, and clarify a definition for the category of "research centers", for better assessment of current site enrollment and data representativeness.

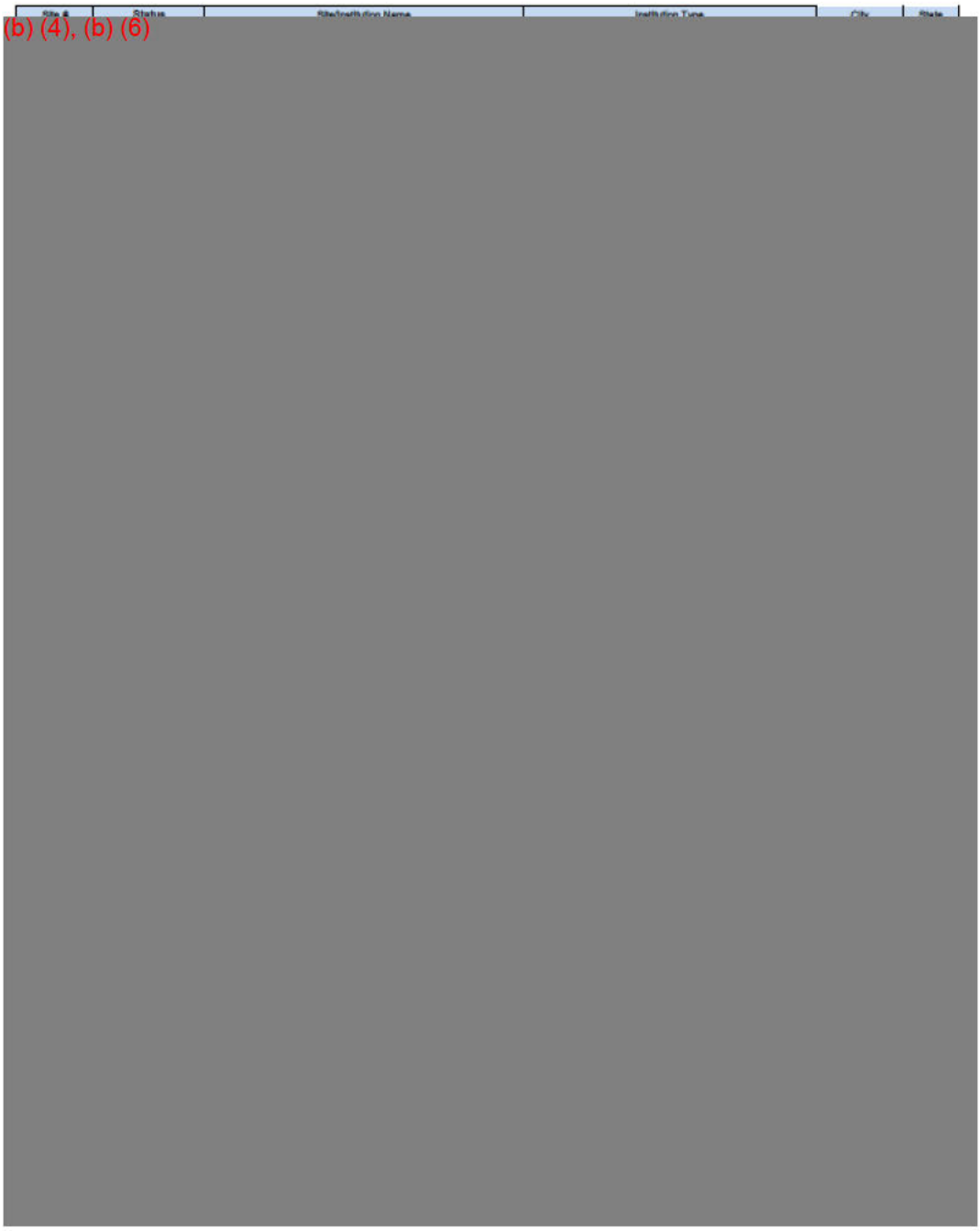
Please reply via email, by October 19, 2017. Please let me know if you have any questions or concerns.

Thank you!
(b)(6)

FDA U.S. FOOD & DRUG ADMINISTRATION

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received:
(b)(4)

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



Attachment 2: Meeting Minutes (December 11, 2017)

Tcon with Bayer

Participants:

FDA: (b)(6)

Bayer: (b)(6)

FDA requested this tcon to discuss two issues:

(b)(4)

Bayer:

(b)(4)

FDA: (b)(4)

Bayer: (b)(4)

**From:** (b) (6)
**Sent:** Friday, January 12, 2018 12:04 PM
**To:** (b) (6)
**Cc:** (b) (6)
**Subject:** RE: PS160001/R2/A1 - Bayer Healthcare, LLC - email receipt - correction

---

**From:** (b) (6)
**Sent:** Friday, January 12, 2018 11:08 AM
**To:** (b) (6)
**Cc:** (b) (6)
**Subject:** - Bayer Healthcare, LLC - email receipt

Trade Name: Essure System for Permanent Birth Control
Document Number: PS160001/R2/A1
Dated: January 4, 2018
Received: January 4, 2018

Dear (b) (6):

Please update your records reflecting the room location for me to received your packages on time.

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received your section 522 postmarket surveillance (PS) changes. Within 60 days of the receipt date, FDA will notify you in writing of the decision.

Please be sure that future correspondence regarding your 522 PS study is sent to the attention of (b) (6). If you have any procedural or policy questions concerning postmarket surveillance requirements, please contact (b) (6)

**Thank you,**

(b) (6)

FDA U.S. FOOD & DRUG ADMINISTRATION

*Excellent Customer Service is important to us. Please take a moment to provide feedback regarding the customer service you have received.*

(b) (4)

**From:** (b) (6)
**Sent:** Wednesday, January 24, 2018 12:54 PM
**To:** (b) (6)
**Cc:** (b) (6)
**Subject:** FDA Decision - Bayer Healthcare, LLC - PS160001/R002 and PS160001/R002/A001

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your section 522 postmarket surveillance (PS) study report PS160001/R002 and PS160001/R002/A001. This report is for the Postmarket Surveillance Study.

We have determined that you have sufficiently met the reporting expectations for the above report. Please be advised that your study status will be marked as "Progress Adequate" on the Section 522 Postmarket Surveillance Studies webpage (www.fda.gov/522studies).

Your next scheduled report is due March 3, 2018.

**Thank you,**

(b) (6)

*Excellent Customer Service is important to us. Please take a moment to provide feedback regarding the customer service you have received.*

(b) (4)

(b) (6)
U.S. Food and Drug Administration
Center for Devices and Radiological Health
(b) (6)
10903 New Hampshire Ave.
WO66-3211

August 31, 2017

Bayer HealthCare
Pharmaceuticals Inc.
100 Bayer Boulevard
P.O. Box 0915
Whippany, NJ 07981-0915
Phone: (b) (6)
Fax: (b) (6)

**RE: Postmarket Surveillance (PS) Study: PS160001/R002**
**12-Month Interim Postmarket Surveillance Report**
Trade Name: Essure System for Permanent Birth Control
Reference PMA: P020014

Dear (b) (6):

Reference is made to FDA's letter dated February 29, 2016 regarding order to conduct a postmarket surveillance study for Essure under Section 522 of the Federal Food, Drug and Cosmetic Act. Reference is also made to FDA's approval of the Essure 522 study plan on September 2, 2016.

Bayer is herewith submitting the 12-month Interim Postmarket Surveillance Report (see **Attachment 1**).

The information contained in this submission is considered confidential, and Bayer therefore requests protection of this information in accordance with 18 USC 1905, 21 USC 331 (1), 5 USC 522.

This submission is provided in accordance with the eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff (October 10, 2013).

Bayer HealthCare Pharmaceuticals certifies that this submission has been scanned for viruses and is virus free using TREND MICRO™ Office Scan™ , Program Version Office Scan™, Program Version 10.6 or higher. For any questions regarding eCopy technical aspects of this electronic submission, please contact (b) (6) or by email at (b) (6)

Bayer looks forward to closely working with the FDA on this post market surveillance study. Should you require additional information, please feel free to contact (b) (6).

Respectfully,

(b) (6)

[redacted]

**ATTACHMENT 1: 12-Month Interim Postmarket Surveillance Report**

cc: (b) (6)

# 12-Month Interim Postmarket Surveillance Report

An open-label, non-randomized, prospective observational cohort study to assess post-procedural outcomes in two cohorts of women who chose to undergo either hysteroscopic sterilization (Essure®) or laparoscopic tubal sterilization

Bayer Study (b) (4)

Postmarket Surveillance
Application #PS160001

Date of Report: 02 SEP 2017

Data Current to:
30 JUN 2017 (data extract)
09 AUG 2017 (site/subject recruitment metrics)

## Table of Contents



## Table of Tables

## List of abbreviations

| | |
|---|---|
| AE | Adverse event |
| FAS | Full analysis set |
| GI | Gastrointestinal |
| IRB | Institutional review board |
| LTS | Laparoscopic tubal sterilization |
| MedDRA | Medical Dictionary for Medical Activities |
| (b) (4) | (b) (4) |
| PSV | Pre-selection visit |
| SAE | Serious adverse event |
| SOC | System organ class |
| TEAE | Treatment-emergent adverse event |

# 1. General Information

Postmarket Surveillance Application Number: PS160001

## 1.1 Sponsor Information

Name: Bayer Healthcare LLC

Address: 100 Bayer Blvd.
P.O. Box 915
Whippany, NJ 07981 USA

Contact Person: (b) (6)

Telephone: (b) (6)
Fax: (b) (6)

Email Address: (b) (6)

## 1.2 Product Information

Device trade name and model number: Essure® System (ESS305)

Date of the 522 order: 29 FEB 2016

Date of postmarket surveillance plan approval: 02 SEP 2016

# 2. Report Information

Date of report: 02 SEP 2017

Data included in this report: clinical study

Type of submission: interim Postmarket Surveillance Report

# 3. Postmarket Surveillance Information

## 3.1 Study Purpose

### 3.1.1 Goals

Study(b) (4) is an open-label, non-randomized, continuous enrollment, prospective observational, postmarket surveillance study of 2 cohorts of subjects who chose to undergo:

- hysteroscopic sterilization (Essure System), or
- laparoscopic tubal sterilization.

### 3.1.2 Objectives

(b) (4)

### 3.1.3 Study Endpoints

(b) (4)

(b) (4)

## 3.2 Study Population

The planned study population includes subjects of reproductive age, between 21 and 45 years of age, who have not been pregnant within the past 6 weeks.

The Essure study population group will include subjects who chose to undergo hysteroscopic sterilization and who meet the criteria as outlined in the most current approved version of the Essure Instructions for Use.

(b) (4)

A sample size of 1400 subjects in each treatment group is planned.

Subjects will be followed for a total of 36 months post-procedure. Table 1 provides the subject follow-up visit schedule.

**Table 1 Subject Follow-up Visit Schedule**

| Time of Visit | Office Visit | Telephone Contact |
|---|---|---|
| (b) (4) | | |

## 3.3 Report Dates

The postmarket surveillance plan was approved by the Food and Drug Administration on 02 SEP 2016. The milestone information regarding site and subject recruitment efforts presented in Section 3.4 is current through 09 AUG 2017.

The data extract used for the tabulations provided in Section 3.5 to Section 3.8 of this report includes all data entered into the database as of 30 JUN 2017. Subjects enrolled between 30 JUN 2017 and 09 AUG 2017 are not included in these tabulations. Data are preliminary and will be updated with ongoing monitoring efforts.

The anticipated study/surveillance completion date is MAY 2023.

## 3.4 Summary of Study/Surveillance Progress Milestones/Timeline Elements

### 3.4.1 Site Recruitment Status

A total of 75 sites is planned. The expected completion date for site enrollment is May 2018. The site enrollment progress as of 09 AUG 2017 is shown below. Based on the progress made since the 02 MAR 2017 6-month surveillance report, the study is on target to achieve the MAY 2018 target date for full site enrollment.

- number of sites contacted: approximately 2531
- number completing Questionnaire #1 (Interest): 182 (140: Yes; 18: Maybe; 24: No)
- number completing Questionnaire #2 (Feasibility): 143
- number identified for pre-selection visit (PSV): 98
- number of PSVs completed: 81
- number of sites approved for participation: 69
- number of IRB approvals: 40
- number of clinical sites activated (approved to begin screening): 34
    - type of facilities:
        - University Hospital: 3
        - Public/Private Hospital: 0
        - Research Center: 31

A summary of subject enrollment by study site is shown in Table 2.

**Table 2 Subject Enrollment by Study Site**

| Site # | Essure | LTS | Total |
|---|---|---|---|
| (b) (4) | | | |

### 3.4.2 Subject Recruitment and Accounting

A total enrollment of 2800 subjects (1400 subjects in each group) is planned. A subject is considered to be enrolled after signing informed consent. The milestones summarized below are based on data current through 09 AUG 2017. Additional data regarding disposition, baseline characteristics, and safety results for the cohort of subjects enrolled as of the 30 JUN 2017 extract date are summarized in Section 3.5 to Section 3.8.

- number of subjects enrolled (signed informed consent): 55
- subject accrual start date: 03 MAY 2017
- number of sites with subjects enrolled: 13 .

- subject accrual completion date: target = OCT 2020
- percentage of subjects reaching each designated study phase: see Table 3
- comparison of target versus actual enrollment and follow-up: first subject enrolled was achieved 3 weeks prior to the target date of 29 MAY 2017 and subsequent subject enrollment is on track with target projections.

**Table 3 Subject Accountability by Treatment Group (As of 09 AUG 2017)**

| Milestone | Essure | Laparoscopic Tubal Sterilization |
|---|---|---|
| Enrolled (signed informed consent) | 30 | 25 |
| Screen-failed | (b)(4) | |
| Screened but no procedure yet | | |
| Had procedure visit | | |
| Procedure | | |
| Attempted | | |
| Not attempted[a] | | |
| Told to rely | | |
| Had 1-week telephone contact | | |
| Had 3-month telephone contact | | |
| Discontinued[a] | | |
| Lost to follow-up | | |
| (b) (4) | | |

## 3.5 Subject Disposition

The disposition of subjects enrolled as of the 30 JUN 2017 data extract is shown in Table 4. Of the [b)(4)] subjects in the Essure group and [b)(4)] subjects in the LTS group who signed informed consent and entered the screening phase, [b)(4)] and [b)(4)] subjects, respectively, had a procedure visit and had the procedure attempted as of 30 JUN 2017 (b)(4) subjects were screen-failed and [b)(4)] subjects were discontinued from the study. [b)(4)] subjects in the Essure group had reached their 3-month confirmation test time point as of the data extract date.

**Table 4 Disposition – Overview (All Enrolled Subjects) (As of 30 JUN 2017)**

| Disposition | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| Number (%) of subjects enrolled | (b) (4) | | |
| Screening Failures | | | |
| Entered Procedure Phase | | | |
| No Procedure Attempted | | | |
| Procedure Attempted | | | |
| Told to Rely | | | |
| Completed the End of Study visit | | | |
| Discontinued from the Study | | | |

(b) (4)

## 3.6 Subject Demographics and Baseline Characteristics

(b) (4)

**Table 5 Demographic Characteristics (Full Analysis Set)**

| | Essure (b)(4) | Laparoscopic Tubal Sterilization (b)(4) | Total (b)(4) |
|---|---|---|---|
| (b)(4) | | | |

Source: Section 5.1

## 3.7 Procedure-Related Findings

(b)(4)

## 3.8 Interim Safety Findings

(b)(4)

(b)(4)

**Table 6 Overall Summary of Adverse Events (Full Analysis Set)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 6 Overall Summary of Adverse Events (Full Analysis Set) (continued)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 6 Overall Summary of Adverse Events (Full Analysis Set) (continued)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

**Table 7 Subject Incidence of Treatment-emergent Adverse Events (TEAEs) by SOC and Preferred Term (Full Analysis Set)**

| | Essure (b)(4) | | Laparoscopic Tubal Sterilization (b)(4) | | Total (b)(4) | |
|---|---|---|---|---|---|---|
| | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) | Number of AEs | Number of Subjects (%) |
| (b)(4) | | | | | | |

## 4. Summary

Study activities related to site and subject recruitment are on track to achieve full site enrollment by MAY 2018 and subject enrollment by OCT 2020. As of the data extract date (30 JUN 2017), (b)(4) ESSURE and (b)(4) LTS procedures had been performed. (b)(4)
(b)(4)

# 5. Appendix

## 5.1 Demographics and Baseline Characteristics (Full Analysis Set)

(b)(4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| [redacted] | | | |

**Demographics and Baseline Characteristics (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Demographics and Baseline Characteristics (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

## Demographics and Baseline Characteristics (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | [redacted] | [redacted] | [redacted] |

## 5.2 Summary of Reproductive and Menstrual History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Reproductive and Menstrual History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

## 5.3 Summary of Contraceptive Method at Baseline (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

## 5.4 Summary of Abdominal/Pelvic Surgical History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Abdominal/Pelvic Surgical History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Summary of Abdominal/Pelvic Surgical History (Full Analysis Set) (continued**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

## 5.5 Medical History (Full Analysis Set)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Medical History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Medical History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | [redacted] | [redacted] | [redacted] |

**Medical History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | [redacted] | | |

## Medical History (Full Analysis Set) (continued)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

**Medical History (Full Analysis Set) (continued)**

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

## 5.6 Prior Medication (Full Analysis Set)

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

**Prior Medication (Full Analysis Set) (continued)**

(b) (4)

| | Essure | Laparoscopic Tubal Sterilization | Total |
|---|---|---|---|
| (b)(4) | | | |

(b) (4)

## 5.7 Adverse Events – Subject Listing (Full Analysis Set)

Treatment Group (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

## Adverse Events – Subject Listing (Full Analysis Set) (continued)

Treatment Group: (b)(4)

| Unique Subject Identifier/ Age/Race | SOC/ Preferred Term / Reported Term | Start Prior to Index Event/ AEOSI | Serious/ Reason | Adverse Event Start Date (Day)/ End Date (Day)/ Duration (days) | Intensity | Relation to Procedure/ Type of Procedure | Treatment of AE | Outcome | Comment |
|---|---|---|---|---|---|---|---|---|---|
| (b)(4) | | | | | | | | | |

Race is identified as: A = Asian, B = Black, W = White, AI = American Indian or Alaska Native, NH = Native Hawaiian or Other Pacific Islander, NR = Not Reported, MUL = Multiple.
The unit of 'Age' is years.
'(Day)' is the day relative to the index event date.
Y=Yes, N=No, AEOSI = adverse event of special interest

**From:** (b) (6)
**Sent:** Tuesday, September 05, 2017 11:58 AM
**To:** (b) (6)
**Cc:** (b) (6)
**Subject:** PS160001/R2 - Bayer Healthcare, LLC - email receipt

Trade Name: Essure System for Permanent Birth Control
Document Number: PS160001/R2
Dated: August 31, 2017
Received: September 1, 2017

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received your section 522 postmarket surveillance (PS) 1 year report. Within 60 days of the receipt date, FDA will notify you in writing of the decision.

Please be sure that future correspondence regarding your 522 PS study is sent to the attention of (b) (6) . If you have any procedural or policy questions concerning postmarket surveillance requirements, please contact (b) (6)

**Thank you,**

(b) (6)

FDA U.S. FOOD & DRUG ADMINISTRATION

*Excellent Customer Service is important to us. Please take a moment to provide feedback regarding the customer service you have received.*
(b) (4)

**From:** (b) (6)
**Sent:** Thursday, October 26, 2017 3:12 PM
**To:** (b) (6)
**Cc:** (b) (6)
**Subject:** FDA Decision - Bayer Healthcare, LLC - PS160001/R2

Dear (b) (6) :

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your section 522 postmarket surveillance (PS) study report PS160001/R2. This report is for the Postmarket Surveillance Study .

We have determined that you have sufficiently met the reporting expectations for the above report. Please be advised that your study status will be marked as "Progress Adequate" on the Section 522 Postmarket Surveillance Studies webpage (www.fda.gov/522studies).

Your next scheduled report is due March 3, 2018.

If you have any questions, please contact me.

**Thank you,**

(b) (6)

FDA U.S. FOOD & DRUG ADMINISTRATION

*Excellent Customer Service is important to us. Please take a moment to provide feedback regarding the customer service you have received.*

(b) (4)