(b)(4)

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(b)(6)

U.S. Food and Drug Administration
Center for Devices and Radiological Health
(b)(6)
10903 New Hampshire Ave.
Silver Spring. MD 20903
(b)(6)

August 30, 2019

(b)(6)
921 Parker Street
Berkeley, CA 94710
Phone: (b)(6)

RE: Postmarket Surveillance (PS) Study: PS160001/R006
36-Month Study 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 36-month Interim Postmarket Surveliance 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)

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)(4) or by email at (b)(6)

Respectfully,

(b)(6)

ATTACHMENT 1: 36-Month Interim Postmarket Surveillance Report

cc: (b)(6)

36-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: 30 AUG 2019

Data Current to:

04 JUL 2019

1. Table of Contents

2. Table of Tables

3. List of abbreviations

AE	adverse event
ERA	event requiring adjudication
FAS	full analysis set
HSG	hysterosalpingogram
LTS	laparoscopic tubal sterilization
MedDRA	Medical Dictionary for Regulatory Activities
PD	protocol deviation
PRO	patient-reported outcomes
(b)(4)	
PSV	pre-selection visit
SAE	serious adverse event
SOC	System Organ Class
TEAE	treatment-emergent adverse event
TVU	transvaginal ultrasound

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: 30 AUG 2019

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 two 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, at least 21 years of age, who have not been pregnant within the past 6 weeks.

The Essure study population group includes 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)

Subjects will be followed for a total of 60 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 or Office Visit
(b)(4)		

3.3 Report Dates

The postmarket surveillance plan was approved by the Food and Drug Administration (FDA) on 02 SEP 2016.

The data extract used for the tabulations provided in this report includes all data entered into the database as of 04 JUL 2019. Data are preliminary and will be updated with ongoing monitoring efforts.

3.4 Summary of Study/Surveillance Progress Milestones/Timeline Elements

3.4.1 Site and Subject Recruitment Status

The site and subject enrollment progress as of 04 JUL 2019 is shown below. A subject is considered to be enrolled after signing informed consent.

- number of sites contacted: approximately 8774
- number completing Questionnaire #1 (Interest): 421 (341: Yes; 50: Maybe; 30: No)
- number completing Questionnaire #2 (Feasibility): 359
- number identified for pre-selection visit (PSV): 133
- number of PSVs completed: 104
- number of sites approved for participation: 90
- number of Institutional Review Board approvals: 74
- number of clinical sites activated (approved to begin screening): 67
    - type of facilities (note: additional categories have been added to this section to reflect the verbatim response provided by sites for type of facility):
        - University Hospital: 12
        - Public/Private Hospital: 4
        - Research Center: 3
        - Private Practice: 30

- Private Practice/Research Center: 11
- Public/Private Hospital/Private Practice/Research Center: 2
- Public/Private Hospital/University Hospital: 1
- Public/Private Hospital/Private Practice: 1
- University Hospital/Research Center: 1
- University Hospital/Private Practice: 1
- Integrated Care System: 1

- number of sites with subjects enrolled: 60
- number of active sites: 57
- subject accrual start date: 03 MAY 2017
- subject accrual completion date: target = to be determined
- number of subjects enrolled (signed informed consent): 952 (Essure: 321; LTS: 631)
- percentage of subjects reaching each designated study phase: see Section 3.4.2.

On 20 JUL 2018, Bayer announced a business decision to discontinue sales of the Essure device effective 31 DEC 2018. Per FDA request, in order to better assess how study enrollment rates change over time with changing device sales, the monthly enrollment from July through December 2018 as a percentage of Essure sales was evaluated and provided in the 30-month report. There have been no sales since December 2018.

3.4.2 Subject Disposition and Accounting

The disposition of subjects enrolled (signed informed consent) as of the 04 JUL 2019 data extract is shown in Table 2. Of the 321 subjects in the Essure group and 631 subjects in the LTS group who signed informed consent and entered the screening phase, (b)(4) and (b)(4) subjects, respectively, attended the procedure visit and of these, (b)(4) and (b)(4) subjects, respectively, had the procedure attempted. (b)(4)

(b)(4)

(b)(4)

A full accounting of subjects by treatment group and study phase is in Table 3.

Table 2 Disposition – Overview (All Enrolled Subjects)

Disposition	Essure	Laparoscopic Tubal Sterilization	Total
Number (%) of subjects enrolled	321	631	952
Screening Failures	(b)(4)		
Primary Reason			
Pregnancy			
Inclusion/exclusion Criteria not met			
Lost to follow-up			
Withdrawal by Subject			
Other			
Entered Procedure Phase			
No Procedure Attempted			
Procedure Attempted			
Confirmation Attempted			
Told to Rely[a]			
Completed the End of Study visit			
Discontinued from the Study			
Primary Reason			
Pregnancy			
Protocol deviation			
Lost to follow-up			
Withdrawal by Subject			
Other[b]			

(b)(4)

Table 3 Subject Accountability by Treatment Group (Full Analysis Set)

Treatment Group: Essure

	Procedure	1 Week	3 Months	12 Months	24 Months	36 Months
Eligible for visit	(b)(4)					
Active						
Visit performed						
Missed visit						
Discontinued						
Lost to follow-up						

Treatment group: Laparoscopic Tubal Sterilization

	Procedure	1 Week	3 Months	12 Months	24 Months	36 Months
Eligible for visit	(b)(4)					
Active						
Visit performed						
Missed visit						
Discontinued						
Lost to follow-up						

(b)(4)

3.5 Subject Demographics, Baseline Characteristics, and Medical History

(b)(4)

Table 4 Demographics, Baseline Characteristics, and Medical History (Full Analysis Set)

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

Table 4Demographics, Baseline Characteristics, and Medical History (Full Analysis Set) (continued; 2 of 3)

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

Table 4 Demographics, Baseline Characteristics, and Medical History (Full Analysis Set) (continued; 3 of 3)

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

3.6 Procedure-Related Findings

(b)(4)

Table 5 Essure Insert Placement Status (Full Analysis Set)

	Essure (b)(4)
(b)(4)	

3.7 Interim Safety Results

(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; 2 of 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; 3 of 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; 4 of 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)						

Table 7 Subject Incidence of Treatment-emergent Adverse Events (TEAEs) by SOC and Preferred Term (Full Analysis Set) (continued; 2 of 18)

	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) (continued; 3 of 18)

	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) (continued; 4 of 18)

	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) (continued; 5 of 18)

	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) (continued; 6 of 18)

	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) (continued; 7 of 18)

	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) (continued; 8 of 18)

	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) (continued; 9 of 18)

	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) (continued; 10 of 18)

	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) (continued; 11 of 18)

	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) (continued; 12 of 18)

	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) (continued; 13 of 18)

	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) (continued; 14 of 18)

	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) (continued; 15 of 18)

	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) (continued; 16 of 18)

	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) (continued; 17 of 18)

	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) (continued; 18 of 18)

	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)						

3.7.2 Events of Special Interest

3.7.2.1 Chronic Lower Abdominal and/or Pelvic Pain

(b)(4)

Table 8 Subject Incidence of Treatment Emergent Chronic Lower Abdominal and/or Pelvic Pain 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)						

3.7.2.2 Abnormal Uterine Bleeding Events

(b)(4)

Table 9 Subject Incidence of Treatment Emergent Abnormal Uterine Bleeding Events 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)						

3.7.2.3 Invasive Gynecologic Surgery

(b)(4)

Table 10 Subject Incidence of Invasive Gynecologic Surgery Post Sterilization Procedure (Full Analysis Set)

	Essure (b)(4)		Laparoscopic Tubal Sterilization (b)(4)		Total (b)(4)	
	Number of Events	Number of Subjects (%)	Number of Events	Number of Subjects (%)	Number of Events	Number of Subjects (%)
[redacted]						

(b)(4)

3.7.2.4 Device Events

(b)(4)

Table 11 Number of Subjects with Device Events by Primary System Organ Class and Preferred Term (Full Analysis Set)

	Essure (b)(4)		Laparoscopic Tubal Sterilization (b)(4)		Total (b)(4)	
	Number of Events	Number of Subjects (%)	Number of Events	Number of Subjects (%)	Number of Events	Number of Subjects (%)
(b)(4)						

3.7.2.5 Adjudicated Allergic/Hypersensitivity Reactions and Autoimmune Disorders

(b)(4)

3.8 Summary of Protocol Deviations

(b)(4)

4. Summary

(b)(4)

(b)(6)

From: (b)(6)
Sent: Thursday, September 5, 2019 10:24 AM
To: (b) (6)
Cc: (b)(6)
Subject: PS160001/R6 - Bayer Healthcare, LLC - email receipt

Trade Name: Essure System for Permanent Birth Control
Document Number: PS160001/R6
Dated: August 30, 2019
Received: September 3, 2019

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) 3 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)

10903 New Hampshire Ave
Silver Spring, MD 20903-0002
(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)

From: (b)(6)
Sent: Monday, November 4, 2019 9:49 AM
To: (b) (6)
Cc: (b) (6)

Subject: FDA Decision Letter, PS160001/R006, Bayer Pharma AG, Essure System for Permanent Birth Control

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/R006. This report is for the study 3 year report for the Postmarket Surveillance Study.

We have determined that you have sufficiently met the reporting expectations for the above report.

Advisory List:
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). Please also consider the following advisories concerning your study report and progress:

(b) (4)

Your next scheduled report is due March 2, 2020.

Thank you,

(b) (6)

(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)

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: November 1, 2019

From: (b) (6)

Subject: PS160001
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: The Record

Through: (b) (6)

Conclusion/Recommendation:
Choose One: The interim report can be accepted
522 Requirement Progress Status: Progress Adequate

Purpose:

The purpose of this memorandum is to present the epidemiologic review for the 36-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 0.8 mm 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

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.

Indication for Use

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

Regulatory History

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.

In July 2018, Bayer notified FDA that they would be discontinuing sales of Essure devices for business reasons. Bayer noted that they would continue to sell Essure through December 31, 2018. (b) (4)

(b) (4)

Due to the discontinuation of sales, the company would be unable to enroll the originally planned number of subjects in the 522 protocol. Therefore, the company submitted a supplement to modify the 522 protocol on (b) (6). The supplement was reviewed by (b) (6)

(b) (6) FDA approved the changes in the protocol, which included the following major modifications:

(b) (4)

(b) (4)

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 who are at least 21 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). Women seeking laparoscopic tubal sterilization must be considered appropriate surgical candidates by the investigator.
Sample Size	952 women from up to 90 sites (321 women in the Essure arm and 631 women in the LTS arm for a 2:1 ratio)
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. Key Endpoints: Pain: The proportion of subjects reporting AEs of chronic lower abdominal and/or pelvic pain after insertion of Essure System (ESS305) (b) (4) Bleeding: The proportion of subjects reporting AEs of abnormal uterine bleeding after insertion of Essure System (b) (4) (b) (4) (b) (4) Total incidence of new onset or worsening abnormal bleeding events will be based on AE reporting.

Study Element	Description
	Hypersensitivity/allergy/autoimmune disorders: The proportion of subjects with adjudicated new onset or (b) (4) allergic/hypersensitivity reactions (b) (4) (b) (4)
	Proportion of subjects undergoing invasive gynecologic surgery (b) (4) (b) (4) including
	Essure insert removal (b) (4) (b) (4)
	Additional endpoints: • Patient reported outcome measures (b) (4) (b) (4) • Rates of AEs
Length of Follow-up and Frequency of Follow-up Assessments	(b) (4) (b) (4) 60 months.
Enrollment Plan and Follow-up Measures	(b) (4)
Statistical Plan	(b) (4)

Study Element	Description
	(b) (4)

Timeline for Study Implementation

(b) (4) The latest study timeline showing below was approved during the review of study protocol change on December 20, 2018.

Milestone	Proposed Timing
Expected date of study initiation	September 2016
Expected monthly number of study sites with IRB approvals	No criterion; aim for 90 sites total
Expected date of initiation of subject enrollment	May 2017
Expected number of subjects enrolled per site per month	No criterion; enrollment of subjects will continue as long as Essure is available for implantation. Expected total patient number by July 2019 is 292 in the Essure arm, with no expected enrollment through December 31, 2019.
Expected date of enrollment completion	December 2019
Expected date of study follow-up completion	December 2024
Expected date of Final Report submission	April 2025

PS Study Interim Status/Results and Assessments:

This report covers the time period of September 2, 2016 through July 4, 2019.

Study Elements
Number of IRB Approvals/sites enrolled

Description: IRB approvals

- As of July 4, 2019: 74 approvals
- As of September 1, 2019 (interactive review): 76 approvals

Description: Sites Enrolled

- As of July 4, 2019: 67 sites activated
- As of September 1, 2019 (interactive review): 67 activated

Assessment

- Since the last interim report (PS160001/R005, data cutoff Jan 4, 2019), the number of IRB approvals and sites enrolled has remained at the same level.
- ***Progress Adequate.***

Number of subjects enrolled

Description

- Enrollment began on May 3, 2017
- As of July 4, 2019: total enrollment of 952 (321 Essure, 631 LTS; LTS to Essure ratio 1.96)
    - The sponsor does not report enrollment as a percentage of sales, as the device is no longer being sold.
- As of September 1, 2019 (interactive review): total enrollment of 1002 (329 Essure, 673 LTS; LTS to Essure ratio 2.0)

Assessment

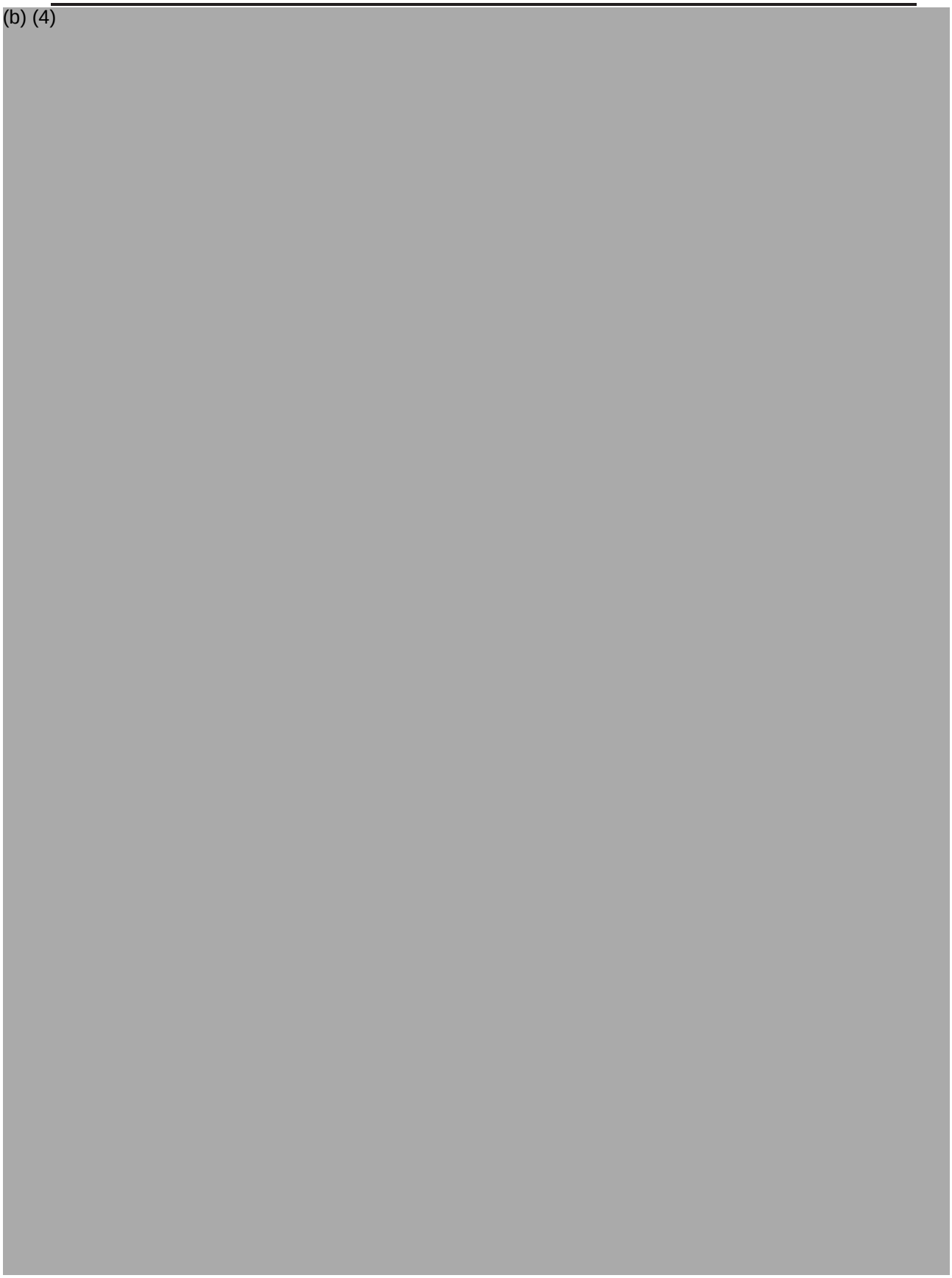
- (b) (4) (b) (4) In addition, it is expected that enrollment continue as long as Essure is being implanted.
- (b) (4) In addition, patients continue to be enrolled after the discontinuation of Essure sales.
- The ratio of LTS to Essure patients is expected to be 2:1. Currently, the ratio is 2.04, which is on target.
- ***Progress Adequate.***

Follow-up rate

Description

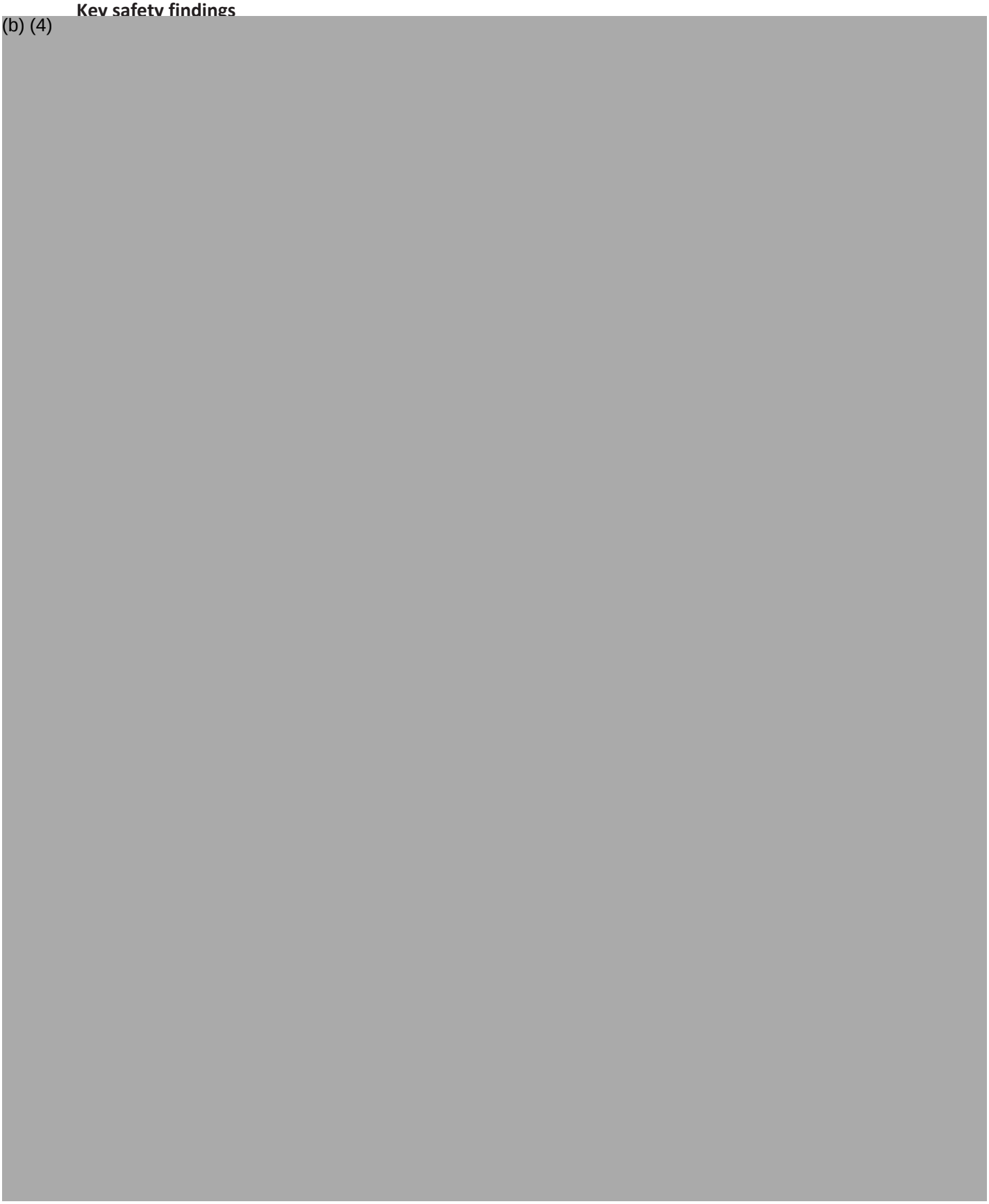
(b) (4)

(b) (4)

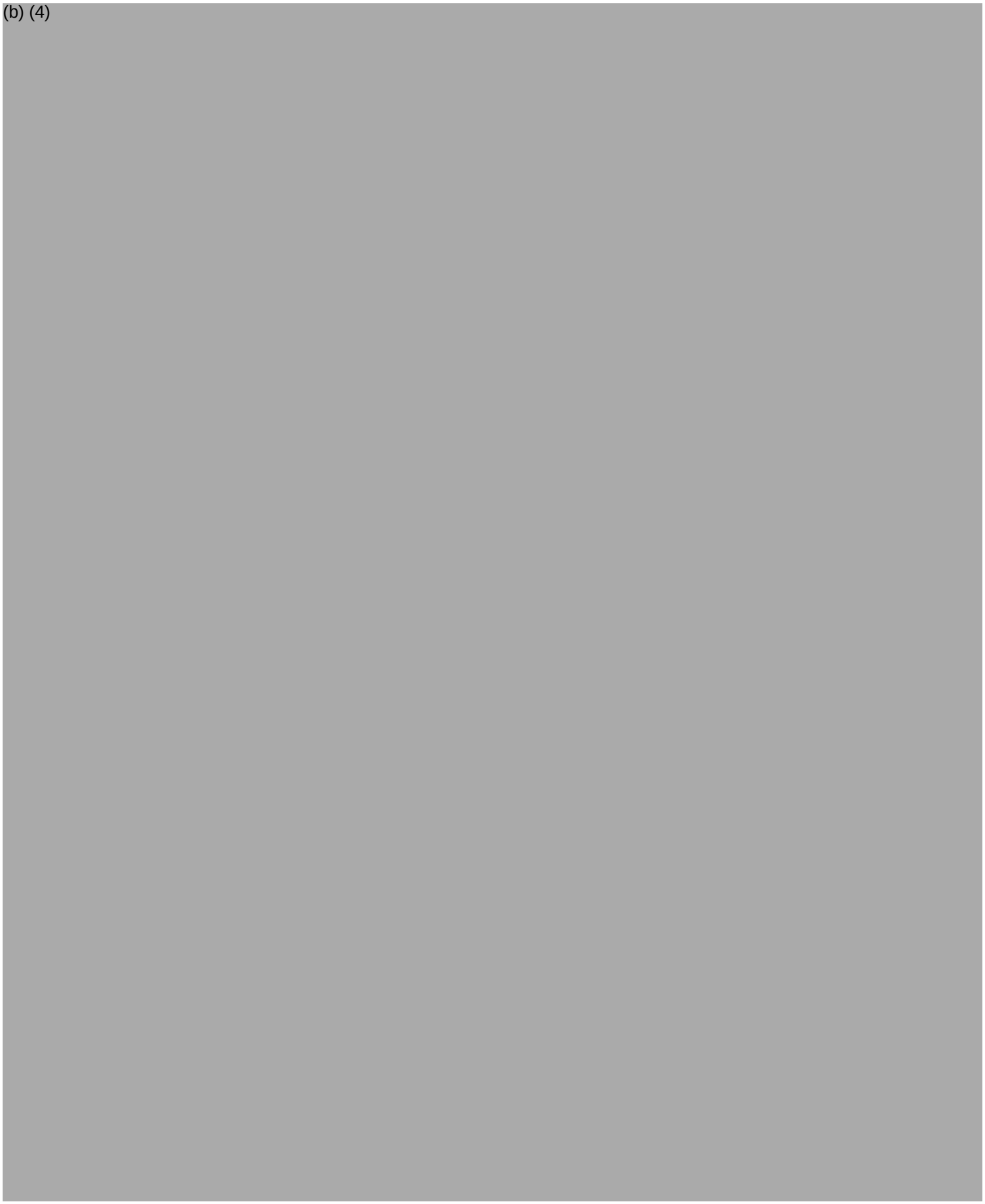


Key safety findings

(b) (4)



(b) (4)



(b) (4)

Summary of Interim Study Results for the 522 Webpage

Study Elements	Description
Number of study sites enrolled	As of September 1, 2019, 1,002 patients have been enrolled (329 in the Essure arm and 673 in the laparoscopic tubal ligation arm).
Number of subjects enrolled	As of September 1, 2019, 67 sites have been enrolled. 61 sites are open for enrollment
Sample Size	On July 20, 2018, Bayer announced that Essure sales would stop in the United States after December 2018. Health Care providers can implant Essure up to one year from the date the device was purchased. The planned sample size of 1,400 women per arm is no longer feasible. The FDA is requiring study enrollment into the Essure arm to continue as long as Essure is available in the U.S. Enrollment into the laparoscopic tubal sterilization arm will stop after it reaches approximately 2:1 ratio with the Essure arm.

In addition, the site will be updated to reflect the new 42month report due March 2, 2020.

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.

■	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

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). Please also consider the following advisories concerning your study report and progress:

(b) (4)

(b) (6)

cc: (b) (6)

Document History:

Date	Activity	Initials
10/24/19	Drafted	(b) (6)
10/28/19	Reviewed with edits	
10/28/19	Finalized	

This template last updated – March 23, 2016
(b) (6) Revised to add interim data elements January 9, 2017
(b) (6) Revised for upload to CDRH Docs,Apr 20, 2017

	(b) (6)
Reviewer's Sign-Off	
Assistant Director Sign-Off	

Appendix 1: Interactive review emails September 5, 12, 16, 17 19, and 20, 2019, and October 1 and 16 2019

Email chain dated September 19, 2019:

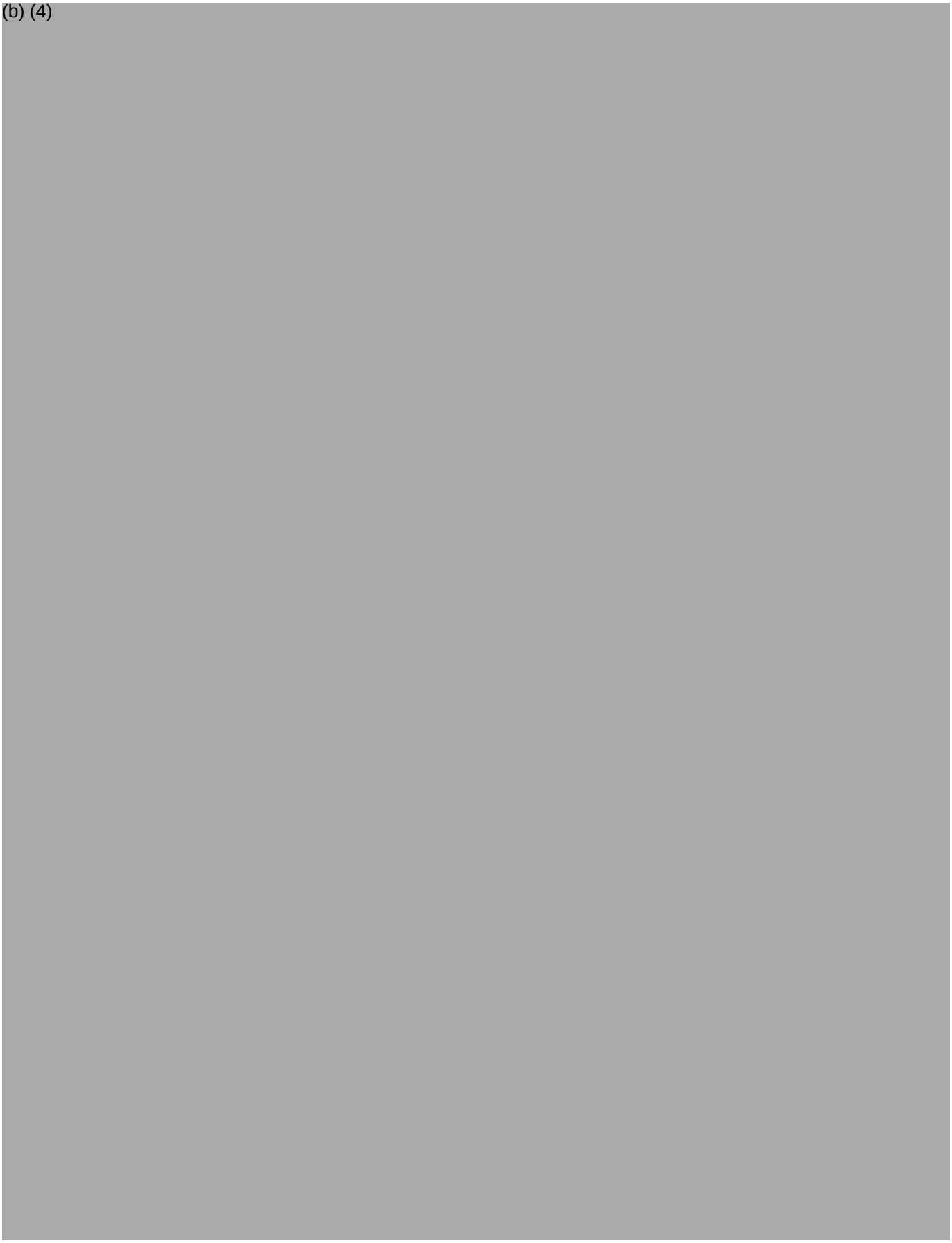
Dear (b) (6)

Please find Bayer's response to your queries regarding the 522 study report.

(b) (4)

(b) (4)

(b) (4)



(b) (4)

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

//////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

Web: http://www.bayer.us

From: (b) (6)
Sent: Thursday, September 12, 2019 10:26 AM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Hi (b) (6)

Thank you very much for the update. I have some additional questions I was hoping you could address:

(b) (4)

Thank you very much. Please let me know if you have any questions regarding the requests.

(b) (6)

(b) (6)

10903 New Hampshire Avenue

Silver Spring, MD 20993

TEL: (b) (6)

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: Click here for survey link

From: (b) (6)
Sent: Thursday, September 12, 2019 10:58 AM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Dear (b) (6)

Below I have included the enrollment update through end of August.

- Number of sites approved for participation: 90
- Number of IRB approvals: 76
- Number of clinical sites activated and open for enrollment: 67 activated, 63 open for enrollment (b) (4)

(b) (4)

Number of sites with subjects enrolled: 59

- Number of subjects enrolled (by arm): Essure – 329; LTS – 673

We are working on the second request and will get that information to you soon.

Thank you,
(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

Web: http://www.bayer.us

From: (b) (6)
Sent: Thursday, September 5, 2019 1:07 PM
To: (b) (6)
Cc: (b) (6)
Subject: Essure 522 report PS160001/R006 - Interactive review

Hi (b) (6)

I just received the 522 report in my queue today (it was technically received 9/3), and have had a chance to take a brief look at the information. I had a couple requests I was hoping you could address as soon as possible:

(b) (4)

Thank you, and please let me know if you have any questions.

(b) (6)

10903 New Hampshire Avenue

Silver Spring, MD 20993

TEL (b) (6)

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please do not directly or indirectly use, print, copy, forward, or disclose any part of this message. Please also delete this e-mail and all copies and notify the sender. Thank you.

The information contained in this e-mail is for the exclusive use of the intended recipient(s) and may be confidential, proprietary, and/or legally privileged. Inadvertent disclosure of this message does not constitute a waiver of any privilege. If you receive this message in error, please do not directly or indirectly use, print, copy, forward, or disclose any part of this message. Please also delete this e-mail and all copies and notify the sender. Thank you.

Email chain dated September 20, 2019:

Dear (b) (6)

(b) (4)

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

//////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

From: (b) (6)
Sent: Tuesday, September 17, 2019 4:46 AM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Hi (b) (6)

(b) (4)

(b) (6)

(b) (6)

10903 New Hampshire Avenue

Silver Spring, MD 20993

TEL (b) (6)

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: Click here for survey link

From: (b) (6)
Sent: Monday, September 16, 2019 1:38 PM
To (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Dear (b) (6)

Attached please find the KM analysis.

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

Web: http://www.bayer.us

Email dated October 1, 2019:

Dear (b) (6)

Below please find the updated information regarding enrollment. The team is working on the request for the narratives. I will provide a timeline as soon as I get it.

- Number of sites approved for participation: 90
- Number of IRB approvals: 76
- Number of clinical sites activated and open for enrollment: 67 activated, 61 open for enrollment (b) (4)

(b) (4)

  - (b)(4)

- Number of sites with subjects enrolled: 59

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

Web: http://www.bayer.us

Email chain dated October 16, 2019:

Dear(b) (6)

Please find the narratives as requested In the attached document.

Kind regards,

(b) (6)

//////////////////////

Bayer AG

Research & Development, Pharmaceuticals

Group WHC 1

Building M085, 320

13353 Berlin, Germany

(b) (6)

Web: http://www.bayer.com

(b) (4)

/// Vorstand: Werner Baumann, Vorsitzender | Liam Condon, Hartmut Klusik, Kemal Malik, Wolfgang Nickl, Stefan Oelrich, Heiko Schipper

/// Vorsitzender des Aufsichtsrats: Werner Wenning

/// Sitz der Gesellschaft: Leverkusen | Amtsgericht Köln, HRB 48248

Von: (b) (6)
Gesendet: Montag, 7. Oktober 2019 22:45
An: (b) (6)
Betreff: RE: Essure 522 removal narratives and clarification on enrollment

Dear (b) (6)

(b) (4) . Bayer will send you the information by October 16th.

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

//////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

(

United States

(b) (6)

Web: http://www.bayer.us

From: (b) (6)
Sent: Monday, September 30, 2019 12:36 PM
To: (b) (6)
Subject: RE: Essure 522 removal narratives and clarification on enrollment

Dear (b) (6)

Below please find the updated information regarding enrollment. The team is working on the request for the narratives. I will provide a timeline as soon as I get it.

- Number of sites approved for participation: 90
- Number of IRB approvals: 76

- Number of clinical sites activated and open for enrollment: 67 activated, 61 open for enrollment (b) (4)

(b)(4) - Quality Control

  - (b)(4)

- Number of sites with subjects enrolled: 59

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

//////////////////////

Bayer U.S. LLC

Development, Pharmaceuticals

Essure & Devices

921 Parker Street

Berkeley CA 94710

United States

(b) (6)

Web: http://www.bayer.us

From: (b) (6)

Sent: Tuesday, September 24, 2019 8:18 AM

To: (b) (6)

Subject: Essure 522 removal narratives and clarification on enrollment

Hello (b) (6)

(b) (4)

(b) (6)

(b) (6)

10903 New Hampshire Avenue

Silver Spring, MD 20993

(b) (6)

FDA U.S. FOOD & DRUG ADMINISTRATION

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Appendix 2: Informal consult from (b) (6), OPEQ/OHT3/DRGUD/ORHT email dated September 23, 2019

(b) (6)

(b) (4)

Interim Safety Results

(b) (4)

(b) (5)

(b) (4)

(b) (4)

Reviewer's Comment

(b) (4)

Thanks,

(b) (6)

(b) (6)

Silver Spring, MD 20993

(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)

Appendix 3: Attachments-(b) (6) Consult Memo and Interactive Review Attachments

Page Blank, see beginning of attachments below.

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

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

MEMORANDUM

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Date: September 30, 2019

From: (b)(6)

Subject: PS160001/R006
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)

Conclusion/Recommendation:
The interim report (PS160001/R006) can be accepted.
522 Requirement Progress Status: Progress Adequate

Purpose:

The purpose of this memorandum is to present the epidemiologic review for the 30-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 (LTS).

Study Element	Description
Study Hypothesis	There is no hypothesis testing.
Study Population	The study population will include subjects of reproductive age, over 21 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). Women seeking laparoscopic tubal sterilization must be considered appropriate surgical candidates by the investigator.
Sample Size	(b) (4) (b) (4), due to the announcement of cessation of sales: Study enrollment into the Essure arm will continue as long as Essure is being implanted in the U.S. Enrollment into the laparoscopic tubal sterilization arm will be ceased once its enrollment reaches approximately 2:1 ratio with the Essure arm.
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. Key Endpoints: Pain: The proportion of subjects reporting AEs of chronic lower abdominal and/or pelvic pain after insertion of Essure System (ESS305) (b) (4) Bleeding: The proportion of subjects reporting AEs of abnormal uterine bleeding after insertion of Essure System (b) (4) (b) (4) (b) (4). Total incidence of new onset or worsening abnormal bleeding events will be based on AE reporting.

Study Element	Description
	Hypersensitivity/allergy/autoimmune disorders: The proportion of subjects with adjudicated new onset or (b) (4) allergic/hypersensitivity reactions (b) (4) (b) (4) Proportion of subjects undergoing invasive gynecologic surgery (b) (4) including Essure insert removal (b) (4) Additional endpoints: • Patient reported outcome measures (b) (4) (b) (4) • Rates of AEs
Length of Follow-up and Frequency of Follow-up Assessments	(b) (4) (b) (4) 60 months.
Enrollment Plan and Follow-up Measures	(b) (4)
Statistical Plan	

Study Element	Description
	(b) (4)

Timeline for Study Implementation (approved on December 20, 2018: (b) (4)

Expected date of study initiation	*September 2016*
Expected date of initiation of subject enrollment	*May 2017*
Expected date of enrollment completion	*December 2019*
Expected date of follow-up completion	*December 2024*
Expected date for final report submission	*Q2 2025*

PS Study Interim Status/Results and Assessments:

Study Elements

Number of IRB Approvals

Description

- As of July 4, 2019: 74
- As of August 31, 2019: 76 (see Attachment 1 for interactive review)

Assessment

- Acceptable

Number of study sites enrolled

Description

- As of July 4, 2019: 67 sites activated, 60 sites with subjects enrolled, 57 active sites
- As of August 31, 2019: 67 sites activated, 63 sites open for enrollment (b) (4)), 59 sites with subjects enrolled

Assessment

- No additional sites have been enrolled since the last interim report. The study has met the initial target number of sites (50-75). **Acceptable.**
- According to the interactive review response, as of August 31, 2019, 67 sites have been activated, and (b) (4) . (b) (4)

Number of subjects enrolled

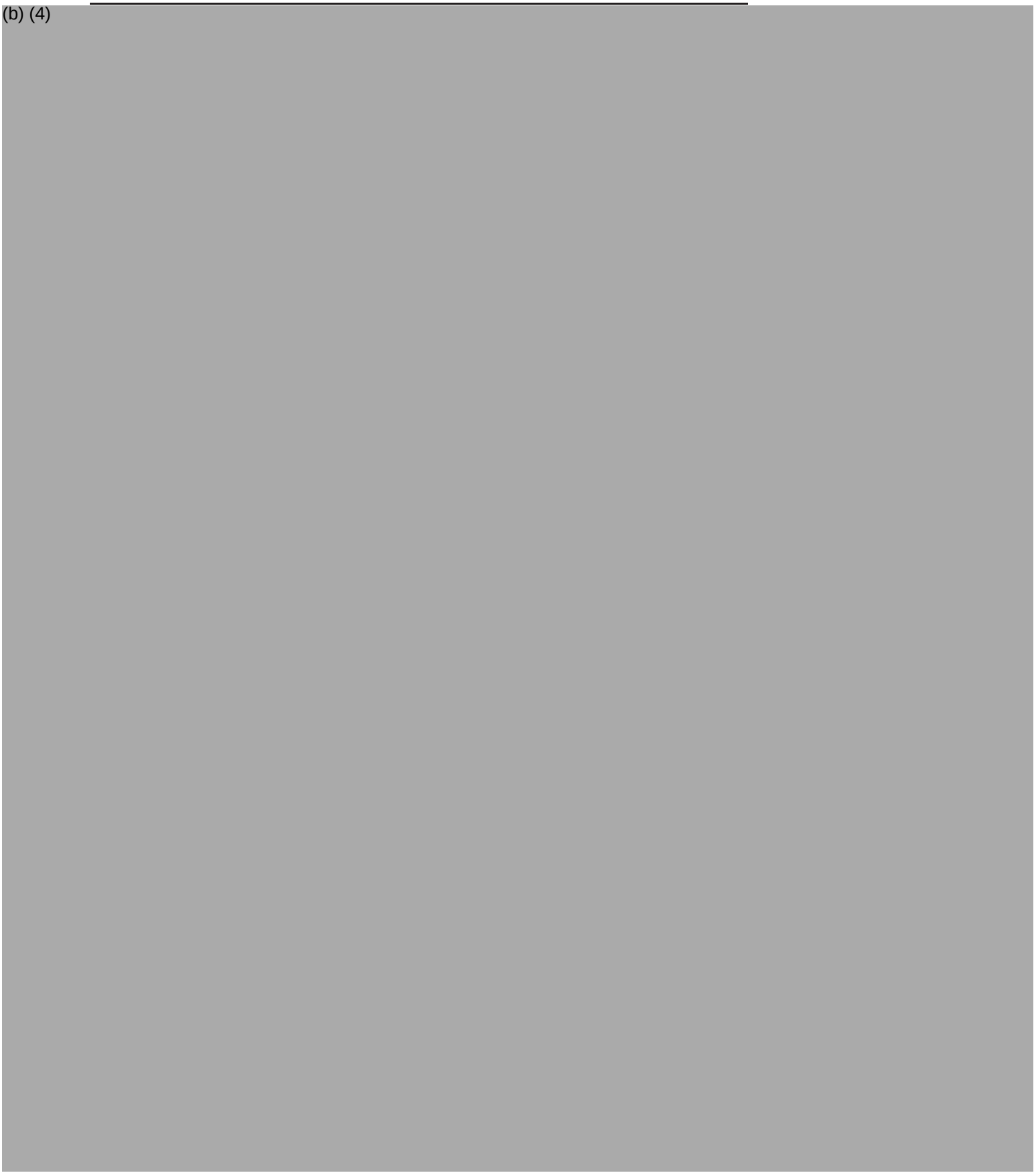
Description

- Enrollment began on May 3, 2017.
- As of Jul
  - (b) (4)
- As of August 31, 2019: 1,002 (Essure: 329, LTS: 673)
- Baseline characteristics of subjects: see Table 4 of submission

Assessment

- On July 20, 2018, the manufacturer publicly announced that sales of Essure will cease after December 31, 2018. (b)(4) (b) (4) (b) (4) Enrollment into both arms has continued, and the ratio of LTS to Essure patients is currently approximately 2:1, as projected. Therefore, progress is adequate.
- The sponsor was advised in a previous interim report (PS160001/R004) to submit the subject enrollment rate as a percentage of device sales in future interim reports. This was not provided in this report; however, there were no sales in 2019. Therefore, this information is no longer needed.
- Table 4 of the submission displays baseline characteristics of both stud arms. (b) (4) (b) (4)

(b) (4)



(b) (4)

Summary of Interim Study Results for the 522 Webpage

Study Elements	Description
Number of study sites enrolled	(b) (4)
Number of subjects 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.

Suggested Deficiency List:

1. (b)(4)

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)

Attachment List

Attachment 1: Interactive Review and Enrollment Update (September 12, 2019)

Attachment 1: Interactive Review and Enrollment Update (September 12, 2019)

From: (b) (6)
Sent: Thursday, September 19, 2019 1:33 PM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Dear (b) (6)
Please find Bayer's response to your queries regarding the 522 study report.

(b) (4)

(b) (4)

(b) (4)

Thank you,

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

////////////////////

Bayer U.S. LLC
Development, Pharmaceuticals
Essure & Devices
921 Parker Street
Berkeley CA 94710
United States
Tel: (b) (6)
Mobile:
E-mail:
Web: http://www.bayer.us

From: (b) (6)
Sent: Thursday, September 12, 2019 10:26 AM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Hi (b) (6)

Thank you very much for the update. I have some additional questions I was hoping you could address:

(b) (4)

Thank you very much. Please let me know if you have any questions regarding the requests.

(b) (6)

10903 New Hampshire Avenue
Silver Spring, MD 20993
TEL: (b) (6)

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. Click here for survey link

From: (b) (6)
Sent: Thursday, September 12, 2019 10:58 AM
To: (b) (6)
Subject: RE: Essure 522 report PS160001/R006 - Interactive review

Dear (b) (6)
Below I have included the enrollment update through end of August.

- Number of sites approved for participation: 90
- Number of IRB approvals: 76
- Number of clinical sites activated and open for enrollment: 67 activated, 63 open for enrollmen (b) (4)

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- Number of sites with subjects enrolled: 59
- Number of subjects enrolled (by arm): Essure – 329; LTS – 673

We are working on the second request and will get that information to you soon.

Thank you

(b) (6)

Freundliche Grüße / Best regards,

(b) (6)

Bayer U.S. LLC
Development, Pharmaceuticals
Essure & Devices
921 Parker Street
Berkeley CA 94710
United States

(b) (6)

Web: http://www.bayer.us

From: (b) (6)
Sent: Thursday, September 5, 2019 1:07 PM
To: (b) (6)
Cc:
Subject: Essure 522 report PS160001/R006 - Interactive review

Hi (b) (6)

I just received the 522 report in my queue today (it was technically received 9/3), and have had a chance to take a brief look at the information. I had a couple requests I was hoping you could address as soon as possible:

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Thank you, and please let me know if you have any questions.

(b) (6)

(b) (6)

10903 New Hampshire Avenue
Silver Spring, MD 20993
TEL: (b) (6)

FDA U.S. FOOD & DRUG ADMINISTRATION

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