SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Thermal Endometrial Ablation Device

Device Trade Name: AEGEA Vapor System™ (including the AEGEA Vapor Probe Procedure Kit, AEGEA Vapor Generator, and AEGEA Vapor Generator Accessory Kit)

Device Procode: MNB

Applicant’s Name and Address: AEGEA Medical, Inc.
2686 Middlefield Road, Suite A
Redwood City, CA 94063

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160047

Date of FDA Notice of Approval: June 14, 2017

II. INDICATIONS FOR USE

The AEGEA Vapor System™ is indicated to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia (excessive uterine bleeding) due to benign causes for whom childbearing is complete.

III. CONTRAINDICATIONS

The AEGEA Vapor System™ is contraindicated for use in the following:

- A patient who is pregnant or who wants to become pregnant in the future. PREGNANCIES FOLLOWING ABLATION CAN BE DANGEROUS FOR BOTH MOTHER AND FETUS.
- A patient with known or suspected uterine cancer or pre-malignant conditions of the endometrium, such as unresolved adenomatous hyperplasia.
- A patient with endometrial hyperplasia as confirmed by histology.
- A patient with any anatomic condition (e.g., history of previous classical cesarean section or transmural myomectomy, including hysteroscopic and/or laparoscopic myomectomy performed immediately prior to the AEGEA Vapor System™ procedure).
- A patient currently on medications that could thin the myometrial muscle, such as long-term steroid use (except for inhaler or nasal therapy for asthma).
• A patient with a uterine length < 6cm (external cervical ostium to internal fundus).
• A patient with a history of endometrial ablation and/or resection (including endometrial ablation/resection performed immediately prior to the AEGEA Vapor System™ procedure) regardless of the modality by which it was performed. REPEAT ABALATION MAY RESULT IN SERIOUS PATIENT INJURY.
• A patient with active genital or urinary tract infection (e.g., cervicitis, vaginitis, endometritis, salpingitis or cystitis) at the time of treatment.
• A patient with bacteremia, sepsis, or systemic infection.
• A patient with an intrauterine device (IUD) currently in place.
• A patient with active pelvic inflammatory disease or known or suspected hydrosalpinx based on history or ultrasound at screening.
• A patient with undiagnosed vaginal bleeding.

IV. **WARNINGS AND PRECAUTIONS**

The warnings and precautions can be found in the AEGEA Vapor System™ labeling.

V. **DEVICE DESCRIPTION**

The AEGEA Vapor System™ is designed to treat pre-menopausal women with excessive menstrual bleeding due to benign causes for whom childbearing is complete. The AEGEA Vapor System™ uses water vapor to ablate the endometrium to reduce future menstrual bleeding. During the procedure, the physician inserts a disposable, handheld device through the cervix and into the uterus to deliver vapor for 120 seconds to ablate the endometrial tissue.

The AEGEA Vapor System™ consists of three (3) major components: the AEGEA Vapor Probe Procedure Kit, the AEGEA Vapor Generator, and the Vapor Generator Accessory Kit. The Vapor Probe Procedure Kit includes a sterile, single-use, disposable Vapor Probe and a non-sterile Supply and Drain Accessory. The Vapor Probe and Vapor Generator are shown in the figure below.

**AEGEA Vapor Generator and Vapor Probe**

The AC-powered Vapor Generator receives water from a de-ionized water supply to provide vapor for treatment. The single-use Supply and Drain Accessory, supplied non-
sterile with the Vapor Probe Procedure Kit, connects to the sterile water source via an intravenous (IV) spike and to the water supply port of the Vapor Generator. Drain lines are used to discard condensed vapor used during the initial vapor pathway sterilization process and during pre-heating of the conduit, as well as to empty the Vapor Generator tank at the end of the procedure.

The Vapor Generator creates water vapor. Its self-sterilization cycle for its vapor path begins automatically and must be completed before each treatment. Upon attachment of the Vapor Probe to the front of the Vapor Generator, the Vapor Generator automatically performs pre-procedure checks of the device. The user then inserts the Vapor Probe transcervically into the uterine cavity and follows the prompts on the Vapor Generator’s touch-screen to inflate the three positioning balloons to seal the uterine cavity.

A Uterine Cavity Integrity Test (Integrity Test) is performed after placement of the Vapor Probe and prior to vapor delivery to ensure there are no leaks in the uterus or cervical canal through which vapor could escape. A Device Lumen Patency Test (Patency Test) is performed after the Integrity Test to confirm the Vapor Probe tip is positioned appropriately and that the Vapor Probe delivery lumen is not blocked by blood or tissue that could have impacted the saline flow rate and results of the Integrity Test. Vapor delivery is initiated only after both tests are passed consecutively.

Vapor is delivered to the uterus for 140 seconds, with a treatment time of 120 seconds. The first approximately 20 seconds of vapor delivery serves to displace saline remaining in the uterus and device lines after the Patency Test. During vapor delivery, the Vapor Generator regulates intrauterine vapor pressure based on feedback from a pressure sensor near the distal tip of the Vapor Probe and monitors temperature via a thermocouple on a positioning balloon.

The Vapor Generator automatically terminates vapor delivery after 120 seconds of treatment and deflates the balloons so that the user can remove the Vapor Probe.

For additional details, please read the Instructions for Use for the AEGEA Vapor System™ and the Operator’s Manual for the AEGEA Vapor Generator.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for the treatment of excessive uterine bleeding due to benign causes. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with her physician to select the method that best meets her expectations and lifestyle. The following alternative practices and procedures are currently available to treat excessive uterine bleeding due to benign causes, in the absence of structural abnormalities such as fibroid tumors or polyps:
**Drug Therapy**

Drug therapy, using estrogen-progesterogen combinations (such as those found in oral contraceptives) or progesterones (progesterone) by themselves, are approaches frequently employed for the treatment of menorrhagia. Other classes of drugs used include androgens such as Danocrine, Gonadotropin-releasing hormone (GnRH) agonists, and non-steroidal anti-inflammatory drugs (NSAIDS). Drug therapy is typically the first order of treatment to alleviate excessive menstrual bleeding. Drug therapies usually require long-term treatment. They are successful for some patients, but for others they are ineffective and may be associated with unpleasant side-effects. This treatment approach does, however, allow a woman to maintain her fertility.

**Dilatation and Curettage (D&C)**

D&C historically has been the treatment of choice for profuse uterine bleeding in women who are hemodynamically unstable and refractory or intolerant to drug therapy. First the cervix is dilated, and then the endometrial lining of the uterine cavity is either scraped by an instrument or removed/evacuated through vacuum aspiration. D&C may reduce bleeding for a few cycles. If a polyp is present and removed, the bleeding may stop. In most cases, D&C does not provide the patient with long-term definitive results.

**Hysteroscopic Endometrial Ablation**

Hysteroscopic endometrial ablation is a surgical procedure which utilizes a resectoscope or operating hysteroscope, a video monitor, a fluid distention medium such as Glycine or Sorbitol, and a surgical ablation device such as an electrode loop, rollerball, or laser to destroy the inner lining of the uterus, the endometrium. The procedure is typically performed under general or regional anesthesia. The cervix must be dilated to accommodate the hysteroscopic instrument, and the uterine cavity must be properly distended. The most common risks associated with hysteroscopic endometrial ablation are hyponatremia from fluid overload, which is a life-threatening condition, and uterine perforation. This treatment is intended for women who no longer desire to maintain their fertility.

**Second Generation “Global” Endometrial Ablation (GEA)**

Second Generation Endometrial Ablation technologies are faster, less complex and, in most cases, allow for a significant reduction in the incidence of complications associated with endometrial ablation, when compared to the “gold standard,” rollerball ablation. There are currently six (6) endometrial ablation systems approved by FDA:
The ThermaChoice Balloon Endometrial Ablation System (Gynecare, P970021) uses thermal energy from heated sterile fluid (5% dextrose in water) contained within a silastic balloon.

The HydroTherm Ablation System (Boston Scientific, P000040) uses USP 0.9% saline heated externally and injected into the uterine cavity.

The Her Option CyroAblation System (Cooper Surgical, P000032) uses cryoablation.

The NovaSure RF Endometrial Ablation System (Hologic, P010013) uses bi-polar RF energy to create heat and destroy the endometrium to a pre-determined depth using tissue impedance.

The Microsulis Microwave Endometrial Ablation System (Microsulis Medical, P020031) uses microwave energy to heat the endometrial layer using a thermocouple at the tip of the device for ablation depth control.

The Minerva Endometrial Ablation System (Minerva Surgical, P140013) uses bi-polar RF energy and ionized argon gas to create heat and destroy the endometrium.

All these therapeutic approaches are intended for women who no longer wish to maintain their fertility.

**Hysterectomy**

The most definitive surgical treatment for menorrhagia is hysterectomy, or complete removal of the uterus. Hysterectomy is a major surgical procedure performed in the hospital (or surgical center) under general anesthesia and is associated with the risks and complications of major surgery. Depending on the technique, it may require a lengthy recovery period.

**VII. MARKETING HISTORY**

The AEGEA Vapor System™ has not been marketed in the United States or any foreign country.

**VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Below is a list of the potential adverse events (e.g. complications) that can occur or have been reported in association with the use of other endometrial ablation systems and may occur with the use of the AEGEA Vapor System™:

- Post-ablation tubal sterilization syndrome
- Pregnancy-related complications
  
  **Note: Pregnancy following any endometrial ablation procedure is dangerous to both the mother and the fetus**
- Thermal injury to adjacent tissue including bowel, bladder, cervix, vagina, vulva and/or perineum, fallopian tubes, ureter
• Perforation of uterine wall
• Hemorrhage
• Uterine necrosis
• Air embolism
• Infection or sepsis
• Complications leading to serious injury or death
• Cervical or vaginal laceration
• Transient change in appearance of the cervical epithelium
• Thermal injury to extremity
• Mechanical bowel injury
• Diarrhea
• Headache

For any endometrial ablation procedure, commonly reported postoperative symptoms include the following:

• Postoperative cramping can range from mild to severe. This cramping will typically last a few hours and significantly decreases by the first day following the procedure.
• When present, nausea and vomiting typically occur immediately following the procedure, are associated with anesthesia, and can be managed with medication.
• Vaginal discharge
• Vaginal bleeding/spotting

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies have been conducted to assess the safety and effectiveness of the AEGEA Vapor System™. The studies included biocompatibility testing, thermal modeling, bench testing, design/hardware verification testing, sterilization validation testing, shelf-life testing, electrical safety testing, and electromagnetic compatibility testing.

A. Biocompatibility Testing

Patient contact with the AEGEA Vapor System™ is either direct by contact (of the Vapor Probe) with mucosal surfaces in the uterus, cervix, and vagina, or indirect (of the Vapor Generator) through water vapor that is used to ablate the uterine lining. Therefore, the AEGEA Vapor System™ contacts mucosal membranes for a limited contact duration (less than 24 hours). Per 10993-1:2009, assessment of the cytotoxicity, sensitization, and irritation potential of the patient contacting components of AEGEA Vapor System is required.
Vapor Probe

The applicant completed the following biocompatibility testing on the patient contacting components of the Vapor Probe:

- Sensitization – Guinea Pig Maximization Test (ISO 10993-10:2010)
- Irritation – Vaginal Irritation Test (ISO 10993-10:2010)

The protocol and results of the above studies are acceptable and demonstrate that the direct patient contacting components of the Vapor Probe are non-cytotoxic, non-sensitizing, and non-irritating.

Vapor Generator

The applicant completed the following biocompatibility testing on the steam condensate samples taken from the Vapor Generator under simulated use conditions:

- Sensitization – Guinea Pig Maximization Test (ISO 10993-10:2010)
- Irritation – Vaginal Irritation Test (ISO 10993-10:2010)

The protocol and results of the above studies are acceptable and demonstrate that the indirect patient contacting components of the Vapor Generator are non-cytotoxic, non-sensitizing, and non-irritating.

B. Thermal Modeling

The applicant performed thermal modeling by numerical simulation to predict the depth of necrosis in tissue resulting from the application of thermal energy generated by the AEGEA Vapor System™. Thermal modeling results correlated with the pathology from extirpated and peri-hysterectomy study results and demonstrated adequate safety.

C. Bench Testing of the Integrity Test System

The Integrity Test System of the AEGEA Vapor System™ conducts the Integrity Test and Patency Test before the water vapor is delivered into the uterine cavity. Integrity Test ensures no leak through which vapor could escape, whereas Patency Test ensures no blockage by blood or tissue in the vapor probe delivery tip. The applicant conducted bench testing to evaluate the performance of the Integrity Test System. The bench Integrity Test was to confirm the ability of the Integrity Test System to detect a leak through which vapor could escape. The bench Patency Test was to confirm the ability of the Integrity Test System to demonstrate that the vapor probe delivery tip was not obstructed by blood or tissue. Both tests met pre-defined design specifications.
D. Extirpated Uteri Studies

The applicant performed extirpated uteri studies to evaluate the performance of the Integrity Test System of the AEGEA Vapor System™. In these studies, the Integrity Test and Patency Test were conducted using extirpated human uteri. In the first study, five (5) extirpated uteri were evaluated to establish test methods. A second study on 12 extirpated uteri was conducted to complete the verification of the saline flow rate thresholds established as pass/fail determinations for the Integrity Test and Patency Test.

| First Extirpated | • The study demonstrated 100% success in the Integrity Test.  
| Uteri Study      | • Pathologic analysis provided confirmation of an absence of serosal thermal damage. |
| Second Extirpated | • The study demonstrated that the Integrity Test was sensitive enough to detect any leak through which water vapor could escape through a uterine perforation to the serosa or through leaks in the cervical seal.  
| Uteri Study      | • A Patency Test confirmed non-occlusion of the vapor probe device tip. |

Results from these studies demonstrated that the Integrity Test is sufficient to detect a leak through which vapor could escape and that the Patency Test confirms that the Vapor Probe device tip is not occluded.

E. Design Verification Study

The applicant conducted bench testing to verify the design of the AEGEA Vapor Probe. The testing aimed at evaluating the overall functionality of the Vapor Probe as well as the product requirement specifications for each sub-component. Since the functionality of the Vapor Probe depends on the Vapor Generator component for a number of specifications, the Vapor Generator was also indirectly tested, as it was used to perform the functional testing. These tests are outlined below.

- **Verification of Dimensions** – The AEGEA Vapor Probe shaft length and diameter, conduit lengths, adjustable collar and stabilizer travel, and inflated balloon lengths and diameters were measured and found to be within pre-defined design specifications.

- **Pressure Sensor Tests** – The integrated pressure sensor was verified against a calibrated pressure sensor and found to meet pre-defined design specifications.

- **Thermocouple Tests** – The AEGEA Vapor Probe thermocouples were verified against a calibrated thermometer and found to meet pre-defined design specifications.

- **Triple Balloon System Tests** – The sealing balloons were able to maintain their geometries when inflated to nominal pressures in accordance with their design specifications. Balloons were able to endure a specified level of excess pressure and specified number of inflations.
• **Flexible Tip Tests** – The flexible tip of the AEGEA Vapor Probe showed no damage after bending or compressive forces were applied. The tip tolerated a pre-specified bending radius without failure prior to simulated use. Following simulated use, the flexible tip was free of functional damage. These tests verified the ability of the Vapor Probe to withstand forces related to insertion and use and met pre-defined design specifications.

• **Vapor Probe Mechanical Tests** – The AEGEA Vapor Probe showed no damage after bending, tensile, or compressive forces were applied. These tests verified the ability of the Vapor Probe to withstand forces related to insertion and use.

• **Vapor Probe Thermal Tests** – The AEGEA Vapor Probe was verified to not exceed safe contact temperatures for patient and user safety. These tests met pre-defined design specifications.

**F. Hardware Verification Study**

The applicant conducted hardware verification testing for the AEGEA Vapor Generator including both internal and external components. These tests are outlined below.

• **Pre-Procedure Sterilization Test** – The AEGEA Vapor Generator only allowed the user to proceed following the successful completion of the validated sterilization cycle in which the vapor pathway met a pre-specified temperature for a specified length of time. The AEGEA Vapor Generator was verified to perform a controlled self-sterilization cycle in order to provide sterile vapor for delivery through the Vapor Probe.

• **Pre-Procedure Functional Test** – The AEGEA Vapor Generator tests the functionality of the Vapor Probe upon connection to ensure proper operation of the temperature, pressure sensor, balloon system, and flow system, prior to continuing with the procedure.

• **Pre-Procedure Safety Tests** – The AEGEA Vapor Generator provided accurate and reliable flow measurements within specifications to deploy the Uterine Cavity Integrity Test and the Device Lumen Patency Tests. The AEGEA Vapor Generator did not deliver vapor without the successful completion of both tests. These tests met pre-defined design specifications.

• **Calorimetry Tests** – The values of energy delivery and output capability of the AEGEA Vapor Generator were measured and found to be within pre-defined design specification.

• **Treatment Complete Test** – The AEGEA Vapor Generator stopped treatment after 120 seconds and the touch screen indicated “Treatment Complete.”
- **Fault Condition Test** – The AEGEA Vapor Generator was verified to stop treatment at specified fault conditions.

**G. Sterilization Validation Study**

The AEGEA Vapor System™ includes the Vapor Generator, a reusable, self-sterilizing device, and the Vapor Probe, a single-use device that is provided sterile. The Vapor Generator Accessory Kit and Supply and Drain Tubing are provided non-sterile and used non-sterile.

**Vapor Probe**

The Disposable Vapor Probe is sterilized to a sterility assurance level of $10^{-6}$ using Ethylene Oxide (EO). Sterilization is performed in accordance with ISO 11135-1:2014: Sterilization of healthcare products and ISO 10993-7: 2008: Biological Evaluation of medical devices. Packaging and pouch seal integrity were tested to ensure sterility following shipping and environmental conditioning.

Bioburden testing was conducted on the AEGEA Vapor Probe Assembly per Annex A of ISO 11737-1:2006. The bioburden found on the AEGEA Vapor Probe Assembly does not present a challenge to the EO sterilization cycle or its efficacy in providing an SAL of $10^{-6}$ for the AEGEA Vapor Probe Assembly. The Ethylene Oxide (EO) and Ethylene Chlorohydrin (ECH) residual levels for the AEGEA Vapor Probe Assembly meet ANSI/AAMI/ISO 10993-7:2008 requirements for limited exposure devices prior to release for distribution.

**Vapor Generator**

The AEGEA Vapor Generator is reusable and packaged non-sterile. The Vapor Generator completes an automated self-sterilization cycle of the vapor path prior to each patient-use. The 2-minute sterilization cycle produces a $10^{-6}$ sterility assurance level in the vapor pathway of the AEGEA Vapor Generator.

**H. Electrical Safety and Electromagnetic Compatibility Testing**

The AEGEA Vapor System™ complies with all applicable subclauses and collateral standards of the following standards related to electrical safety and electromagnetic compatibility:


I. Software Verification and Validation Testing

The applicant provided software information for the AEGEA Vapor System™ in accordance with the FDA guidance document “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices” issued on May 11, 2005. In accordance with this guidance, the software used in AEGEA Vapor System™ has a major level of concern.

J. Shelf-Life

The applicant has proposed a 6-month shelf-life for the Vapor Probe based on the results of an accelerated aging study. The accelerating study demonstrates that the Vapor Probe maintains its functionality and its packaging maintains the sterility of the device for a shelf-life of six (6) months.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed three (3) clinical studies as follows:

- Peri-hysterectomy Study
- Feasibility Study
- Pivotal Clinical Study (protocol SE-3000)

1. Peri-hysterectomy Study

The applicant conducted two (2) peri-hysterectomy studies at one investigational site to evaluate the safety and the ablation parameters of the AEGEA Vapor System™. In these studies, women who were scheduled for an abdominal hysterectomy underwent endometrial ablation with the AEGEA Vapor System™ just prior to hysterectomy.

The first study enrolled ten (10) women who underwent endometrial ablation. The Integrity Test and Patency Test were performed prior to delivery of vapor in all subjects. There were no reported device- or procedure-related adverse events. Gross pathology and histology examinations revealed no evidence of transmural myometrial perforation or serosal thermal injury in any uteris. The cavity ablation coverage and the thermal depth of tissue injury were sufficient to support feasibility of the device for treatment of menorrhagia.

The second study enrolled ten (10) women who underwent endometrial ablation prior to hysterectomy. This study measured the serosal surface temperature of the mid- and distal regions of the fallopian tubes during endometrial ablation. The temperatures remained within a safe physiological range. There were no reported device or procedure-related adverse events.
Results from these studies show that the AEGEA Vapor System™ performed as intended and had a safety profile that supported ongoing clinical use.

2. Feasibility Study

The applicant conducted a feasibility study to evaluate the safety and effectiveness of the AEGEA Vapor System™ to reduce menstrual blood loss in women with a history of menorrhagia due to benign causes.

Three (3) sites in The Netherlands enrolled twenty-one (21) subjects, per study protocol entry criteria, who underwent endometrial ablation with the AEGEA Vapor System™. There were no device-related adverse events. One subject experienced an adverse event related to spinal anesthesia, requiring hospitalization post-procedure. Fourteen (14) patients reported uterine cramping in the time period of 24 hours to two (2) weeks following treatment. All adverse events were resolved. Post-treatment cramping is associated with all commercially available endometrial ablation procedures.

The primary effectiveness endpoint, defined as menstrual blood loss reduction to ≤80ml, as measured by the alkaline hematin (AH) assay, was achieved in 95% (18/19) of subjects at 12 months. Data were not available for two (2) of the patients at the 12-month visit. Results from this study are supportive of use of the AEGEA Vapor System™ in the intended patient population.

3. Pivotal Clinical Trial (Protocol SE-3000)

The applicant performed a pivotal clinical study to establish a reasonable assurance of safety and effectiveness of endometrial ablation with AEGEA Vapor System™ for its labeled indication, ablation of the endometrial lining of the uterus in premenopausal women with menorrhagia (excessive uterine bleeding) due to benign causes for whom childbearing is complete. The study was conducted under IDE #G130128. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The study was a prospective, single-arm, non-randomized, multicenter, open label clinical study. The purpose of the study was to evaluate the safety and effectiveness of the use of the AEGEA Vapor System™ in pre-menopausal women with menorrhagia (excessive menstrual bleeding) for whom childbearing was complete. There were fourteen (14) investigational sites in the United States, Mexico, Canada, and The Netherlands.

One hundred fifty-five (155) patients, which are referred to as Pivotal subjects or Intent-to-Treat (ITT) population, were enrolled in this study. Patients were treated between May 2014 and May 2015. Follow-up visits occurred at 24 hours,
2 weeks, and 3, 6, and 12 months post-procedure. The database for this PMA reflected 12-month followup data collected through June 2016. The primary safety and effectiveness outcomes were analyzed based on ITT population.

Before 155 Pivotal subjects were enrolled, sixty-six (66) patients were treated using an earlier version of the device, and followed for their safety results for three (3) or six (6) months. This study is called the “Safety Study,” and the patients are referred to as “Safety subjects.” Safety results from the Safety subjects were considered as part of the evaluation of device safety.

The safety endpoint included device- or procedure-related serious adverse events and the overall rate and severity of all reported adverse events.

The primary effectiveness endpoint was reduction in menstrual blood loss as measured by a validated Pictorial Blood Loss Assessment Chart (PBLAC) score of \( \leq 75 \) at one year following the endometrial ablation procedure. The Pictorial Blood Loss Assessment Chart (PBLAC), is a semi-objective method for the assessment of periodic blood loss. It is a self-administered pictorial chart that allows the user to record the number of sanitary pads and tampons used, taking into account the degree to which the items are soiled with blood, passage of blood clots, and episodes of flooding.

Secondary effectiveness endpoints included improvement of quality of life, patient satisfaction, and the need for medical or surgical intervention to treat abnormal bleeding in the 12 months following the ablation procedure.

The effectiveness of the AEGEA Vapor System™ was compared to an FDA established objective performance criterion (OPC) and therefore did not have an active Control Group in the study. The OPC was developed by FDA with input from industry and members of the Obstetrics and Gynecology Devices Panel. The OPC approach used data from the pivotal clinical trials of five (5) approved endometrial ablation systems. These five (5) studies were randomized, controlled trials that used the same active control (rollerball ablation) and had similar patient populations. The study sizes ranged from 260 patients to 322 patients with either a 1:1 randomization or a 2:1 (device:control) randomization scheme. The primary endpoint was reduction in menstrual blood loss as assessed by PBLAC. The inclusion criteria required a baseline PBLAC score of \( \geq 150 \) (four (4) studies) or \( > 185 \) (one study), and individual patient success was defined as a PBLAC score of \( \leq 75 \) at 12 months post procedure. The ITT population consisted of all patients who presented on the day for either the endometrial ablation device or rollerball ablation. Patients with missing PBLAC scores at 12 months were treated as failures. A study was considered a success, if the proportion of successes in the Global Endometrial Ablation (GEA) group met a pre-specified non-inferiority margin compared to the proportion of success in the rollerball ablation control group.
Using a generalized linear mixed model with study as a random effect, the FDA determined that the average success rate across the five (5) GEA devices was 75.6% (65.6%, 83.5%) and 77.2% (66.5%, 85.2%) for the rollerball ablation control. The FDA performed additional analyses to evaluate the effect of baseline covariates on the primary endpoint, including (subject age above and below 40 years), baseline PBLAC score (over 150), uterine sound (6 to 12 centimeters), and presence of fibroids (<3 cm). Using analysis of covariance methods, the FDA found that none of these baseline covariates had a significant impact on the study results. Based on this analysis, the FDA developed a minimum success rate for effectiveness known as an objective performance criterion (OPC). The OPC is 66% based on the lower bound of the 95% confidence interval of the average success rate for the five (5) approved GEA devices.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the AEGEA Pivotal Clinical Trial was limited to patients who met the following inclusion criteria:

- Female subject from (and including) age 30 to 50 years
- Self-reported history of heavy menstrual bleeding in at least 3 of the last 6 months
- Predictable cyclic menstrual cycles over past 6 months
- Excessive uterine bleeding
- Premenopausal at enrollment
- Normal PAP
- Normal endometrial biopsy
- Willing to use reliable contraception

Patients were not permitted to enroll in the AEGEA Pivotal Clinical Trial if they met any of the following exclusion criteria:

- Pregnant
- Desires future childbearing
- Presence of an intrauterine device (IUD)
- Previous endometrial ablation procedure
- Evidence of sexually transmitted infections (STI)
- Evidence of pelvic inflammatory disease (PID)
- Active infection of genitals, vagina, cervix, uterus or urinary tract
- Active endometritis
- Active bacteremia, sepsis or other active systemic infection
- Gynecologic malignancy
- Endometrial hyperplasia
- Known clotting defects or bleeding disorders
- On anticoagulant therapy
- Hemoglobin <8gm/dl
• Prior uterine surgery
• Currently on medication that could thin myometrial muscle
• Severe dysmenorrhea, secondary to adenomyosis
• Abnormal uterine cavity
• Hydrosalpinx
• Uterine length <6cm or >12cm
• Currently in other clinical trial

2. Follow-up Schedule

All Pivotal subjects were scheduled to return for follow-up examinations at 24 hours, 2 weeks, and 3, 6, and 12 months postoperatively.

Preoperatively, each subject completed a self-reported diary to record the number of sanitary products used and menstrual blood loss using PBLAC during their entire menstrual cycle for a single month. This was to ensure the subject had a minimum PBLAC score of ≥150 for study inclusion. Subjects also completed the validated Menorrhagia Impact Questionnaire (MIQ) and Aberdeen Menorrhagia Severity Scale (AMSS) at baseline.

Postoperatively, each subject completed the PBLAC diary at 3, 6, and 12-month follow-up to record the number of sanitary products used and menstrual blood loss during their entire menstrual cycle. The MIQ and AMSS were also completed at those time points. Adverse events were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the primary endpoint was occurrence of adverse events. The applicant evaluated safety by determining the rate (number and percentage) of subjects who experienced one or more device- or procedure-related serious adverse events (SAEs) and overall rate (number and percentage) and severity of all reported adverse events.

With regards to effectiveness, the primary effectiveness endpoint was menstrual blood loss as assessed by PBLAC method. An individual patient was considered a success if her PBLAC score was ≤75 at 12 months post-treatment. An individual patient was considered a failure if she did not meet success criteria.

With regard to success/failure criteria, to achieve study success, the lower bound of the 95% confidence interval should exceed the 66% OPC developed by the FDA.
The secondary endpoints included an analysis of the need for surgical or medical intervention to treat abnormal bleeding, quality of life using the Menorrhagia Impact Questionnaire, and patient satisfaction 12 months after treatment.

B. Accountability of PMA Cohort

At the time of database lock, of 155 patients (Pivotal Subjects) enrolled in the PMA study, 91% (141) were available for analysis at 12 month post-operative visit. Table 1 below summarizes subject disposition.

Table 1: Pivotal Subject Disposition

<table>
<thead>
<tr>
<th>Intent to Treat (ITT) Analysis Cohort</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapor Ablation Attempted</td>
<td>155</td>
</tr>
<tr>
<td>No Treatment Received</td>
<td></td>
</tr>
<tr>
<td>Integrity Test did not pass</td>
<td>2</td>
</tr>
<tr>
<td>Patency Test did not pass</td>
<td>4</td>
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<tr>
<td>Modified ITT (mITT) Analysis Cohort</td>
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<tr>
<td>All ITT subjects who completed the</td>
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<tr>
<td>treatment</td>
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<tr>
<td>Incomplete treatment</td>
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<td>Lost to follow-up</td>
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<td>Suicide</td>
<td>1</td>
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<tr>
<td>Hysterectomy for pain</td>
<td>1</td>
</tr>
<tr>
<td>IUD for heavy bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Major protocol deviations</td>
<td>2</td>
</tr>
<tr>
<td>Per Protocol (PP) Analysis Cohort</td>
<td>141</td>
</tr>
<tr>
<td>All mITT subjects who completed 12-month follow-up</td>
<td></td>
</tr>
</tbody>
</table>

C. Study Population Demographics and Baseline Parameters

The demographics of the study population (Pivotal subjects) are typical for an endometrial ablation study performed in the United States. Table 2 below provides the baseline demographic and gynecological history parameters. Seventy-six (76) patients were 30-39 years old, and 79 patients were 40-50 years old. The mean age of subjects at baseline was 39.8. An evaluation of these data confirmed the data could be pooled across sites and countries.
Table 2. Demographics and Gynecological History

<table>
<thead>
<tr>
<th>Age</th>
<th>Patient number = 155</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (median)</td>
<td>39.8 ± 5.2 (40.0)</td>
</tr>
<tr>
<td>Range (min, max)</td>
<td>(30, 50)</td>
</tr>
<tr>
<td>N Age 30-39</td>
<td>76 (49.0%)</td>
</tr>
<tr>
<td>N Age 40-50</td>
<td>79 (51.0%)</td>
</tr>
</tbody>
</table>

**Ethnicity**
- Hispanic or Latino: 36 (23.2%)
- Not Hispanic or Latino: 119 (76.8%)

**Race**
- American Indian or Alaska Native: 0 (0.0%)
- Asian: 3 (1.9%)
- Black or African American: 5 (3.2%)
- Native Hawaiian or Other Pacific Islander: 0 (0.0%)
- White: 147 (94.8%)

**BMI, kg/m^2**
- Mean ± SD (median): 30.0 ± 7.4 (29.0)
- Range (min, max): (18, 51)

**Gravidity**
- Mean ± SD (median): 3.2 ± 1.7 (3.0)
- Range (min, max): (0, 13)

**Parity**
- Mean ± SD (median): 2.6 ± 1.3 (3.0)
- Range (min, max): (0, 7)

**Menstrual History**
- Dysmenorrhea: 132 (85.2%)

**PBLAC Score at Baseline**
- Mean ± SD (median): 320.7 ± 155.9 (278.3)
- Range (min, max): (153.0, 865.8)

**FSH (IU/L)**
- Mean ± SD (median): 6.2 ± 3.7 (5.3)
- Range (min, max): (0.10, 21.2)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the pivotal ITT cohort of 155 patients for the 12-month evaluation and safety ITT cohort of 66 patients/procedures available for the 3-month evaluation. In the safety ITT cohort, 36 of 66 patients progressed to six (6) months follow-up before the protocol was amended to limit follow up to 3 months. The key safety outcomes for this study are presented below in Table 3, which shows the number and percentage
of patients who reported device- or procedure-related adverse events, one or more times, during the 12-month follow-up period.

Table 3. Pivotal Subjects Number and Percentage of Subjects with One or More Related\textsuperscript{a} Adverse Events through 12 months

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Day of ablation</th>
<th>Day 1 after ablation</th>
<th>&gt;Day 1 to &lt;2 weeks</th>
<th>&gt;2 weeks to 1 year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine cramping</td>
<td>53 (34.2%)</td>
<td>3 (1.9%)</td>
<td>2 (1.3%)</td>
<td>6 (3.9%)</td>
<td>62\textsuperscript{b} (40.0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (6.5%)</td>
<td></td>
<td></td>
<td></td>
<td>10 (6.5%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5 (3.2%)</td>
<td></td>
<td></td>
<td></td>
<td>5 (3.2%)</td>
</tr>
<tr>
<td>Vaginal infection</td>
<td>1 (0.6%)</td>
<td>3 (1.9%)</td>
<td>1 (0.6%)</td>
<td></td>
<td>4\textsuperscript{b} (2.6%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (2.6%)</td>
<td></td>
<td></td>
<td></td>
<td>4 (2.6%)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td></td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Endometritis</td>
<td></td>
<td>2 (1.3%)</td>
<td></td>
<td></td>
<td>2 (1.3%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Back pain over SI joint</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Difficulty with defecation or micturition (urination)</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Fever</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Urinary tract infection (UTI)</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>External vaginal itching</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Lightheadedness</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Spotting</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Intermittent Vaginal Spotting</td>
<td></td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Prolonged Spotting</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Hematometra</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Low back pain</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Menometrorrhagia</td>
<td>1 (0.6%)</td>
<td></td>
<td></td>
<td></td>
<td>1 (0.6%)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Possible, probable or definitely related to device or procedure
\textsuperscript{b} Subjects with more than one occurrence of same event are only counted once

Table 4 below shows the overall adverse events for the Safety Subjects. There were no reported serious adverse device effects (SADEs) nor any reported serious adverse events (SAEs) that were procedure related.
Table 4. Safety subjects Number and Percentage of Subjects with One or More Relateda Adverse Events by Time of Occurrence through 6 months

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Day of Ablation</th>
<th>Day 1 after Ablation</th>
<th>&gt;Day 1 to ≤2 weeks</th>
<th>&gt;2 Weeks to 3 months</th>
<th>&gt;3 months to 6 months b</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine cramping</td>
<td>32 (48.5%)</td>
<td>1 (1.5%)</td>
<td></td>
<td>1 (2.8%)</td>
<td>34 (51.5%)</td>
<td></td>
</tr>
<tr>
<td>Vaginal infection</td>
<td></td>
<td></td>
<td>3 (4.5%)</td>
<td>1 (1.5%)</td>
<td>4 (6.1%)</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (3.0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 (3.0%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (3.0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 (3.0%)</td>
</tr>
<tr>
<td>Cough</td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Transient redness on buttock</td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Spotting</td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Endometritis</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Uterine tenderness</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
<td></td>
<td></td>
<td>1 (1.5%)</td>
</tr>
</tbody>
</table>

aPossible, probable or definitely related to device or procedure.

b36 patients were followed at 6 months.

2. Primary Effectiveness Results

The analysis of effectiveness was based on the 155 evaluable patients (ITT Pivotal subjects) at the 12-month time point. Key effectiveness outcomes are presented in Tables 5.

Based on the success rate of 78.7% (122/155) with a 95% confidence interval (CI) of (72.3%, 85.2%) observed in the ITT population, the 12-month follow-up success rate observed with the AEGEA Vapor System was demonstrated to be statistically significantly greater than the OPC of 66% (p value = 0.0004).

In addition to the primary success criterion of PBLAC ≤75, analyses were also completed to evaluate amenorrhea (PBLAC=0).

Table 5 below summarizes the effectiveness outcomes.

Table 5. Effectiveness by Analysis Cohort at 12-Month Follow-up1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ITT (N=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBLAC ≤75</td>
<td>122 (78.7%)</td>
</tr>
<tr>
<td>Amenorrhea (no menses)</td>
<td>30 (19.4%)</td>
</tr>
</tbody>
</table>

1PBLAC outcomes, including the amenorrhea outcome (PBLAC=0) represent the most recent menses within ± 8 weeks of the 12-month follow-up.
3. Secondary Effectiveness Results

Need for Surgical or Medical Intervention

No subjects required surgical intervention to treat ongoing heavy menstrual bleeding; however one subject had a medical intervention (insertion of an IUD) to treat ongoing heavy menstrual bleeding prior to her 12-month visit.

Quality of Life

The Menorrhagia Impact Questionnaire (MIQ) was administered at baseline and follow-up to assess quality of life. The baseline mean score of 14.7 reduced by 8.1 on average to a mean score of 6.6 at month 12 (change from baseline 95% Confidence Interval (CI) (-8.7, -7.6)). These data are presented below in Table 6.

Table 6. Quality of Life Improvement (MIQ)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=141)</th>
<th>Month 12 (N=141)</th>
<th>Change from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ±SD (median)</td>
<td>14.7 ± 42.9 (15.0)</td>
<td>6.6 ± 1.8 (6.0)</td>
<td>-8.1 ± 3.4 (-8.0)</td>
</tr>
<tr>
<td>Range (min, max)</td>
<td>(6, 21)</td>
<td>(4, 15)</td>
<td>(-15, 0)</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td></td>
<td>(-8.7, -7.6)</td>
</tr>
</tbody>
</table>

Patient satisfaction 12 months after treatment

Subjects were asked to report their overall satisfaction with the ablation procedure. The data show that 90.8% (128/141) were either satisfied or very satisfied at the 12-month follow-up visit. These data are presented below in Table 7.

Table 7. Patient Satisfaction at Month 12

<table>
<thead>
<tr>
<th>Satisfaction Response</th>
<th>Month 12 (N=141)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Satisfied or Satisfied</td>
<td>128 (90.8%); 95% CI (84.8%, 95.0%)</td>
</tr>
<tr>
<td>Very Satisfied</td>
<td>99 (70.2%)</td>
</tr>
<tr>
<td>Satisfied</td>
<td>29 (20.6%)</td>
</tr>
<tr>
<td>Not Sure</td>
<td>10 (7.1%)</td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>3 (2.1%)</td>
</tr>
<tr>
<td>Very Dissatisfied</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

4. Subgroup Analyses

There were 43.2% (67/155) of ITT subjects who had one or more prior C-sections and 56.8% (88/155) who did not have a prior C-section at the time of
endometrial ablation. As shown below in Table 8, 80.6% (54/67) of women with a prior C-section and 77.3% (68/88) without a prior C-section in the ITT analysis cohort met the study success criteria of PBLAC ≤75. These data demonstrate that women with prior C-sections achieved similar outcomes in menstrual bleeding reduction when compared to women without prior C-sections.

Table 8. 12-month PBLAC ≤75 in Subjects with and without C-Section

<table>
<thead>
<tr>
<th></th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>With C-Section</td>
<td>54/67 (80.6%)</td>
</tr>
<tr>
<td>Without C-Section</td>
<td>68/88 (77.3%)</td>
</tr>
<tr>
<td>All Subjects</td>
<td>122/155 (78.7%)</td>
</tr>
</tbody>
</table>

5. **Pediatric Extrapolation**

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. **Financial Disclosure**

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 14 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. **PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION**

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Obstetrics and Gynecology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. **CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES**

A. **Effectiveness Conclusions**

In the pivotal study to support approval, 78.7% (122/155) of subjects in the ITT analysis cohort had a PBLAC score ≤75 12 months after the endometrial ablation procedure. This is statistically significantly greater than the OPC of 66% (p-value = 0.0004).
B. Safety Conclusions

The risks of the device are based on data collected in clinical studies conducted to support PMA approval as described above.

The safety profile for the patient appears favorable based on the outcomes of the pivotal study. There were no serious device or procedure-related adverse events reported. Most of the adverse events occurred within two (2) weeks of the procedure and were resolved without clinical sequelae. The most common adverse events included uterine cramping, vaginal infection, and anesthesia related events.

Patients can be expected to experience a non-serious adverse event, most occurring within the initial two (2) weeks of the procedure. Serious events are expected to be rare (i.e., 1%). The most serious adverse events anticipated with any global endometrial ablation system (e.g., thermal injury to bowel and sepsis) would manifest two (2) weeks of the procedure and would require aggressive management including possibly major surgery and/or intensive care.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical studies conducted to support PMA approval as described above. The benefit of the AEGEA Vapor System™ is a reduction in menstrual blood loss. At 12-months 78.7% (122/155) of women who underwent attempted vapor ablation met the study definition of success and experienced a reduction in menstrual blood loss from excessive to normal or less than normal. In addition, improvement in subjective quality of life scores and high patient satisfaction provide further evidence of probable participant benefit. Based on the available clinical performance outcomes, the risks associated with the AEGEA Vapor System™ are modest and similar to risks associated with approved global endometrial ablation systems.

Additional factors to be considered in determining probable risks and benefits for the AEGEA Vapor System™ include: Heavy menstrual bleeding is a common gynecologic condition that has the potential to adversely affect quality of life. The device design and procedure are not novel and are familiar to the intended user. The ability to undergo an office-based treatment that does not require general anesthesia and allows a rapid recovery is a probable benefit of major value. The data from this multicenter, single arm study are sufficiently robust and are likely repeatable in a population similar to the study cohort.

1. Patient Perspectives

Although patient reported outcomes were collected for both the primary and secondary effectiveness endpoints, the submission did not include specific information on patient perspectives for this device.
In conclusion, given the available information above, the data support that for ablation of the endometrial lining of the uterus in pre-menopausal women with menorrhagia (excessive menstrual bleeding) due to benign causes for whom childbearing is complete, the probable benefits outweigh the probable risks.

D. **Overall Conclusions**

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Given the performance characteristics, device-type (procedure) familiarity, and labeling mitigations, the probable benefits outweigh the probable risks for the AEGEA Vapor System™.

Additionally, the applicant intends to obtain long-term (two- and three-year) safety and effectiveness data from subjects in the ITT cohort who received a complete ablation (120 seconds of vapor treatment) procedure, completed 24 and/or 36 month follow-up and have no major protocol deviations that would render the subject data unevaluable. The labeling for the AEGEA Vapor System™ will be revised with this information when it becomes available.

The reported clinical outcomes from these studies and long-term follow-up plan are adequate for premarket approval.

XIII. **CDRH DECISION**

CDRH issued an approval order on June 14, 2017. The final conditions of approval cited in the approval order are described below.

ODE Lead PMA Post-Approval Study – AEGEA Pivotal Clinical Study (Protocol SE-3000): The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The AEGEA Pivotal Clinical Study is a prospective, single-arm, non-randomized, multicenter, open label study conducted at eleven (11) sites in the United States and three (3) sites outside the United States to evaluate the safety and effectiveness of the AEGEA Vapor System. The study includes 155 pre-menopausal women with menorrhagia (excessive uterine bleeding) due to benign causes for whom childbearing is complete. The one-year outcome data from this study were provided premarket. The two- and three-year outcomes from this study will be provided postmarket and will consist of the following:

- Need for surgical or medical intervention to treat abnormal bleeding
- Subject self-report of pregnancy
- Contraception status (data will be collected at three years only)
- Menstrual status
- Gynecologic adverse events
- Quality of Life Questionnaire
• Patient Satisfaction

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. **APPROVAL SPECIFICATIONS**

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.