

Section I. Clinical Data Report: Pivotal Trial

A. Executive Summary

Introduction

Provided in this introductory section is a description of the unintended pregnancy and abortion rates in the United States as well as the complications associated with pregnancy, the documented need for contraceptive alternatives, a discussion of the risks associated with current methods of permanent birth control (female sterilization), and the unique characteristics of the Essure System for Permanent Birth Control.

Unintended Pregnancy/Abortion Rates

Unintended pregnancy is a significant public health issue that affects not only the woman involved, but also society as a whole. The significance of this public health need is evidenced by the signing into law of Title X of the Public Health Service Act, which provides for a comprehensive federal program devoted entirely to providing family planning services on a national basis.

Using data from the 1982, 1988 and 1995 cycles of the National Survey of Family Growth, supplemented by data from other sources, it has been estimated that almost half (48%) of all pregnancies in the United States in 1994 were unintended, and 54% of these ended in abortion¹. In 1994 alone, there were an estimated 3,000,000 unintended pregnancies, with an estimated half (48%) of women aged 15-44 having had at least one unplanned pregnancy sometime in their lives¹. Although teenagers have the highest rate of unintended pregnancy, the second highest rate is found in women aged 40-44². Furthermore, the rate of

¹ Henshaw SK. Unintended Pregnancy in the United States. *Family Planning Perspectives*, 1998, 30(1): 24-29 & 46.

² Global Health Options.

unintended pregnancies in the U.S. has declined little over the past several decades, and remains higher than other developed nations².

In 1997, over one million abortions were performed, and an estimated 43% of women will have at least one abortion by the time they are 45 years old¹. Abortion is not just an issue that faces teenagers. In fact, based on a 1994-1995 national survey of almost 10,000 abortion patients, over 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women who were age 30 or over³.

Maternal Risks of Pregnancy

According to the CDC⁴, approximately 6 million American women become pregnant each year, and more than 10,000 give birth each day. Two to three women die each day from a pregnancy-related complication, and the maternal mortality rate has not declined since 1982⁴. The leading causes of maternal deaths are hemorrhage, blood clot, high blood pressure, infection, strokes, amniotic fluid in the bloodstream, and cardiomyopathy. It should be noted that the risk of pregnancy-related death rises after the age of 35⁵. In addition to mortality resulting from pregnancy, the CDC states that more than one in three pregnant women in the U.S. develop a pregnancy-related complication⁴. The most common complications include: miscarriage, ectopic pregnancy, hemorrhage, infection, diabetes, high blood pressure, excessive vomiting, premature labor, need for Caesarean delivery, and depression. Furthermore, based on 1986-1987 data from the National Hospital Discharge Survey (NHDS), an estimated 22.2 per 100 hospitalizations involving a birth were non-delivery

³ Henshaw SK. Abortion Patient in 1994-1995: Characteristics and Contraceptive Use. *Family Planning Perspectives*, 28: 140-147 & 158, 1996.

⁴ CDC's Reproductive Health Information Source. *Safe Motherhood: Promotion Health for Women Before, During, and After Pregnancy* 2002.

⁵ CDC Press Release: Fact Sheet, Pregnancy-Related Mortality.

related hospitalizations of pregnant women⁶. Hospitalization for a pregnancy-related complication required an average of >2 million hospital days of care per year and cost >1 billion dollars annually⁶. The authors of this study provided a nationwide estimation of serious pregnancy-related morbidity following childbirth: 62,400 readmissions occurred during the postpartum period, yielding an average annual rate of 8.1 readmissions per 1,000 deliveries.

As stated by the CDC, childbirth remains the most common reason for hospitalization in the U.S., and complicated pregnancies result in more costly hospitalizations. Thus, since women who have unintended pregnancies are less likely to have appropriate prenatal care, more likely to have entry into prenatal care at a later stage of the pregnancy, and are at an increased risk of domestic violence⁷, they are presumably at higher risk of complications and account for more costs related to pregnancies.

Risks to Infant/Child

The National Commission to Prevent Infant Mortality has stated that: “Infant mortality could be reduced by an estimated 10 percent if all women not desiring pregnancy used contraception.”⁸. Similarly, a review by the U.S. Institute of Medicine of the research on this topic concluded that “the child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development⁹. The CDC also states that an infant from an unintended pregnancy has an increased risk of low birth rate, neonatal mortality, risk of SIDS, and developmental problems⁷.

Clearly, there is a significant public health issue represented by these facts and figures.

⁶ Franks AL. Hospitalization for pregnancy complications, United States, 1986 and 1987. *Am J Obstet Gynecol* 1992; 166:1339-44.

⁷ Koonin LM. Promoting Healthy Pregnancies: Counseling and Contraception. September 20, 2000.

⁸ Alan Guttmacher Institute. Title X and the U.S. Family Planning Effort.

⁹ Alan Guttmacher Institute. Family Planning Improves Child Survival and Health. 1998.

Need for Contraceptive Alternatives

Based on data from the 1995 National Survey on Family Growth, it has been suggested in the literature that the high rates of unintended pregnancy reflect dissatisfaction with current methods¹⁰. In addition, based on a 64-country survey, it has been shown that the prevalence of contraceptive use rises with increased access to a variety of contraceptive methods¹¹.

The 1995 National Survey on Family Growth provided data on the current profile of contraceptive use in the United States based on a survey of almost 7,000 women. The survey revealed that the percentage of women discontinuing contraceptive use for method-related reasons within 12 months of method initiation was 44%¹⁰. In addition, during the lifetime of a typical woman who uses reversible methods of contraception, she will discontinue use for a method-related reason 9.5 times. If women using sterilization are included as well, the typical woman will discontinue use of a contraceptive for a method-related reasons only 7.2 times during her lifetime. The survey also found that the typical woman will experience 1.8 unintended pregnancies. If women using sterilization are included as well, the typical woman will experience 1.3 unintended pregnancies. The survey also noted that 6% of sexually active women were not using a contraceptive, which translates to approximately 3.5 million women at risk of unintended pregnancy. Indeed, of the 6 million pregnancies that occurred that year, nearly half were unintended, and more than half of these unintended pregnancies occurred among women who were using contraceptives.

The need for contraceptive alternatives has been acknowledged in recent years not only in the published literature, but also at meetings of the FDA's OB/GYN

¹⁰ Trussel J. Contraceptive Failure, Method-Related Discontinuation and Resumption of Use: Results from the 1995 National Survey of Family Growth. *Family Planning Perspectives*, 1999, 31(2): 64-72 & 93.

¹¹ Ross J. Contraceptive Method Choice in Developing Countries. *International Family Planning Perspectives*, 2001, 28(1): 32-40.

Advisory Committee. Additionally, the need for less invasive transcervical methods of sterilization has been a primary research focus for the USAID Office of Population, Family Health International (FHI), the CONRAD Program, and the WHO Human Reproduction Program.

In introductory remarks to the panel convened in October of 1996 for the review of the PMA for the Lea's Shield, Mr. Pollard (Chief, Obstetrics and Gynecology Devices Branch, FDA) stated: "I would like to add at this point that FDA is responsive to the concerns of women's advocacy groups across the U.S. Many of these groups are very concerned about the limited number of contraceptive options available to women and believe that FDA should be re-examining its review standards for evaluation of these products. This need for more contraceptive options was most recently emphasized in the report that just issued from the Institute of Medicine entitled 'Contraceptive Research and Development: Looking to the Future', highlighting the high rate of unintended pregnancies in the U.S. and worldwide."

In addition, the FDA convened a meeting of the panel in October of 1999 to discuss the requirements for vaginal barrier contraceptive devices to "recalibrate our premarket entry process and optimize the balance of premarket and postmarket requirements" for these devices, as stated by Mr. Pollard. This was largely driven by the results of the 1995 National Survey on Family Growth. Mr. Pollard presented to the panel some of the results discussed above from the survey regarding high rates of unintended pregnancy, abortion, and discontinuation of contraception due to method-related reasons, and went on to state: "To us, at FDA, that describes a huge unmet need." While the focus of the panel meeting was for vaginal barrier contraceptive devices rather than tubal occlusion devices, the underlying motivation for convening the meeting still pertains to consideration of the Essure System: the large unmet need in the area of contraceptive alternatives for women.

The author of the published findings of the 1995 Survey concluded that the high pregnancy rates in the survey “do not reflect the inherent efficacy of methods when used correctly and consistently, but instead reflect imperfect use because most reversible methods are difficult to use correctly.” The author went on to state: “such high rates of discontinuation almost surely reflect dissatisfaction with current methods.”

Prevalence of Tubal Sterilization

Currently, women must choose between temporary reversible methods, with all the limitations discussed above, and permanent birth control (sterilization), with its attendant invasiveness, morbidity, and mortality. Discussed below is the prevalence of tubal sterilization as a contraceptive choice, as well as the risks associated with this method.

Tubal sterilization is the most prevalent method of birth control in the United States. From 1994-1996, more than 2,000,000 tubal sterilizations were performed, for an annual incidence of 11.5 per 1,000 women, or 684,000 per year¹². As noted by Dr. Carolyn Westhoff at a recent meeting on transcervical sterilization sponsored by ARHP, this may well be an underestimate due to the difficulty in capturing the data in recent years.

All currently approved methods of tubal sterilization require access to the peritoneal cavity, and therefore carry the inherent risk associated with invasive surgery. Half of the tubal sterilizations are performed immediately post-partum and are done via mini-laparotomy or laparotomy¹³. The other half represent “interval” sterilizations, 89% of which are done laparoscopically¹³. Therefore, a slight majority of tubal sterilizations are performed by mini-

¹² MacKay AP. Tubal Sterilization in the United States, 1994-1996. *Family Planning Perspectives*, 2001, 33(4):161-166.

¹³ ACOG Technical Bulletin #222 – April 1996. Sterilization.

laparotomy/laparotomy. Currently, laparoscopy is predominantly performed with general anesthesia and involves one or more punctures of the abdominal wall for insertion of a laparoscope; the tubal ligation procedure is then performed through the puncture sites in the abdomen. Both laparotomy and mini-laparotomy are more extensive procedures and require relatively longer recovery periods than laparoscopic methods. About 93 percent of the procedures in the U.S. are performed in a hospital or surgi-center under general anesthesia, with laparoscopic procedures requiring an average of 4-5 hours of hospital recovery time¹⁴, an average of 4-6 days before returning to regular activities, not including the day of surgery^{15,16}, and an average of 3 days before returning to work¹⁶. For procedures performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

Risks with Tubal Sterilization – Mini-Laparotomy/Laparotomy

The Centers for Disease Control and Prevention (CDC) CREST study¹⁸ reported on a subgroup of almost 300 women who underwent interval tubal sterilization by laparotomy. In this subgroup, a major complication rate of 5.7% was reported¹⁷, which was comprised of febrile morbidity and re-hospitalizations. Re-hospitalization occurred for the following reasons: pelvic abscess, pulmonary abscess, pulmonary embolus, bowel obstructions, staph wound infection at site of laparotomy incision, etc. The mean length of postoperative hospital stay was increased by 1.9 nights for women who had at least one complication as compared to those without complication¹⁷. This does not include the additional

¹⁴ Bordahl PE. Laparoscopic Sterilization Under Local or General Anesthesia? A Randomized Study. *Obstet Gynecol* 1993; 81: 137-41.

¹⁵ Fraser RA. The prevalence and impact of pain after day-care tubal ligation surgery. *Pain* 39 (1989) 189-201.

¹⁶ Garcia FA. Economic and Clinical Outcome of Microlaparoscopic and Standard Laparoscopic Sterilization, A Comparison. *J Reprod Med* 2000; 45:372-376.

¹⁷ Layde PM. Risk Factors for Complications of Interval Tubal Sterilization by Laparotomy. *Obstet Gynecol* 62:180, 1983.

¹⁸ Peterson HB. The Risk of Pregnancy after Tubal Sterilization: Findings from the U.S. Collaborative Review of Sterilization. *Am J Obstet Gynecol* 1996; 174:1161-70.

hospitalization experienced by women who were readmitted following their initial discharge. The mean total convalescence period from the time of the surgery until the resumption of normal activities was increased by 8.3 days (from 9.6 days) among women experiencing a complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparotomy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (1.8%), primary incision complications (12.6%), infections (1.1%), and “other” (3.3%). The total complication rate in this study, for the complications reported, was 18.8%. In a similar study comparing the Filshie Clip with the Tubal Ring under laparotomy²⁰, the following complications were noted: surgical injuries (7.3%), primary incision complications (13.9%), infections (0.9%), and “other” (1.4%). The total complication rate in this study, for the complications reported, was 23.5%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional approach.

Risks with Tubal Sterilization – Laparoscopy

Based on data from the CREST study involving over 9,000 women who underwent tubal sterilization by laparoscopy, major complications occurred at a rate of 1.6%, with unintended laparotomy as the most frequent complication²¹. Laparotomies were performed for the following reasons: unexpected bleeding, hematoma formation, viscous perforation (stomach and bowel), and fallopian tube resection. Rehospitalization occurred for the following reasons: pelvic infections, heavy vaginal bleeding, abdominal/pelvic pain, urinary tract infection,

¹⁹ Dominik R. Two Randomized Controlled Trials Comparing the Hulka and Filshie Clips for Tubal Sterilization. *Contraception* 62 (2000) 169-175.

²⁰ Sokal D. Two Randomized Controlled Trials Comparing the Tubal Ring and Filshie Clip for Tubal Sterilization. *Fertility and Sterility*. Vol 74, No 3, September 2000.

²¹ Jamieson DJ. Complications of Interval Laparoscopic Tubal Sterilization: Findings from the United States Collaborative Review of Sterilization. *Obstet Gynecol* 2000; 96:997-1002.

peritonitis caused by bowel burn, bowel obstruction, etc. In an early report based on the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, the median postoperative hospital stay increased from 0 nights for women with no complications to 2 nights for women who had at least 1 complication²². The occurrence of a complication also increased the median total convalescence from 4 days to 14 days. More than one third (36%) of women who developed a complication had a total convalescence longer than 21 days, compared to only 2% of women with no complication.

In addition to the CREST study, in a randomized trial involving almost 900 women who underwent tubal sterilization by laparoscopy using either the Filshie Clip or the Hulka Clip¹⁹, the following complications were noted: surgical injuries (0.8%), primary incision complications (7.9%), infections (0.08%), and “other” (2.5%). The total complication rate in this study, for the complications reported, was 11.2%. In a similar study comparing the Filshie Clip with the Tubal Ring via laparoscopy²⁰, the following complications were noted: surgical injuries (2.2%), primary incision complications (4.4%), infections (0.4%), and “other” (1.0%). The total complication rate in this study, for the complications reported, was 8%. While most of the complications in these two studies of the Filshie Clip were minor incision complications, virtually all would be avoided with a non-incisional method.

Finally, a large prospective study involving over 24,000 women who underwent tubal ligation using one of 5 methods²³ was conducted. In this study, the rate of surgical difficulties, which included anesthesia and equipment problems, etc., ranged from 2.4% to 12.5% (5.1% overall). The rate of surgical complications, which included uterine perforation, bowel injury, artery/vein injury, bladder injury, ovarian injury, etc., ranged from 0.7% to 2.7% (1.7% overall). The rate of

²² Destefano F. Complications of Interval Laparoscopic Tubal Sterilization. *Obstet Gynecol* 61:153, 1983.

²³ Bhiwandiwalla PP. A Comparison of Different Laparoscopic Sterilization Occlusion Techniques in 24,439 Procedures. *Am J Obstet Gynecol* 144:319, 1982.

technical failures, which required a change to a different technique or abandoning the procedure, ranged from 0.6% to 1.0% (0.8% overall).

Risks of Tubal Sterilization – Local vs. General Anesthesia

Based on early reports of the CREST study, involving 3,500 women who underwent tubal sterilization by laparoscopy, a fivefold difference in complication rates was found between procedures performed under general anesthesia and those performed under local anesthesia²². In subsequent reports from the CREST study involving over 9,000 women, use of general anesthesia was found to be a predictor of complications in women undergoing interval laparoscopic tubal sterilization²¹. In addition, 40% of the deaths attributable to tubal sterilization followed complications associated with general anesthesia, and there were no deaths due to complications from local anesthesia²⁴.

In a randomized, controlled trial comparing tubal ligation performed under local anesthesia to general anesthesia in 125 women, total procedure/post-surgery time was significantly shorter in the local anesthesia group¹⁴. In addition, the general anesthesia group had significantly more abdominal pain during the hospital stay, and use of analgesics immediately after surgery was more extensive. Also, the “awakeness” score was higher in the local anesthesia group the same evening as the procedure. Similar to these findings, in another randomized study comparing laparoscopic tubal ligation performed under local vs. general anesthesia²⁵, women in the local anesthesia group had a slightly shorter anesthesia time and recovery room stay. In addition, women in the general anesthesia group were 2.3 and 1.5 times more likely to have maximum systolic and diastolic blood pressures above 160 and 90 mmHg, respectively. They were also 5.7 times more likely to have a maximum heart rate of 110 or higher.

²⁴ Peterson HB. Deaths Attributable to Tubal Sterilization in the United States, 1977 to 1981. *Am J Obstet Gynecol* 146:131, 1983.

²⁵ Peterson HB. Local Versus General Anesthesia for Laparoscopic Sterilization: A Randomized Study. *Obstet Gynecol* 70:903, 1987.

Although use of local anesthesia for tubal sterilization is associated with a lower rate of complications, laparoscopic tubal sterilization still requires access to the peritoneal cavity with its associated risks.

Tubal Sterilization Risks – Pain/Return to Normal Activities

Finally, in a study of over 50 women using validated measures to assess the incidence, intensity and duration of pain following tubal ligation performed laparoscopically, it was found that 85% of women reported that pain and/or fatigue impacted their recovery and contributed to an average delay of return to normal activity level of 4.4 days, not including the day of the procedure. The most powerful predictor of return to normal activity was the total amount of pain experienced. A separate study of 50 women undergoing laparoscopic tubal sterilization similarly found that the average number of days to resume normal activities was 4-6¹⁶. Also, as stated above, when tubal sterilization is performed by laparotomy, total convalescence averaged almost 10 days for women without a complication and almost 18 days for women who experienced a complication¹⁷.

A New Contraceptive Alternative – The Essure System

Given the high unintended pregnancy, abortion and discontinuation rates associated with temporary methods of birth control, and the significant complications that can occur with the invasive surgery currently required for permanent birth control, we believe that women would benefit from a new contraceptive alternative that offers a less invasive method to achieve permanent birth control. As evidence of patient interest in such an alternative, is the statement made by a patient advocacy group to the FDA's OB/GYN Advisory Committee (panel). In February of 1996, Ms. Cindy Pearson, Program Director of the National Women's Health Network addressed the panel, which was convened to review the PMA for the Filshie Clip, stating: “. . .So we just wanted

to communicate a general sense that women are interested in alternative methods of sterilization. In particular, women are interested in methods that offer a safety or convenience advantage over the methods that are currently available to them.”.

The Essure System offers transcervical placement of the Essure Micro-insert, which can be accomplished without incisions or general anesthesia, with no loss of method effectiveness as compared to incisional tubal sterilization. Since the data that follow in this report demonstrate that this can be done safely and effectively to provide permanent birth control, we believe that this alternative will be embraced by women and their physicians, and will offer a significant public health benefit as a result.

Summary

In summary, due to the following points, we believe that there is strong evidence of the need for a new contraceptive alternative for women, especially a permanent method that can be performed without incisions or general anesthesia:

- ?? An estimated half (48%) of pregnancies that occur in the United States each year are unintended, translating to an estimated 3,000,000 unplanned pregnancies in the United States each year.
 - The age group that has the second highest rate of unintended pregnancy is women aged 40-44.

- ?? An estimated half of all unintended pregnancies result in abortion, translating to an estimated 1,000,000 abortions each year in the United States.
 - 45% of the abortions occurred among women who were age 25 or over, and 24% occurred among women over 30 years old.

- ?? The morbidity associated with pregnancy is not infrequent or insignificant to the women or to society.

?? There has been a documented risk to infants and children due to unintended pregnancies.

?? Deaths and major complications occur with currently available methods of tubal sterilization due to general anesthesia and invasion of the peritoneal cavity that is associated with current methods.

We believe that many of the unintended pregnancies and abortions each year could be avoided if women had a permanent birth control option with an alternative risk/benefit profile than current methods.

Executive Summary of Clinical Data

Detailed data on the Pivotal Trial conducted to establish a reasonable assurance of safety and effectiveness for the Essure System are provided in the following sections. This section provides an Executive Summary of the data.

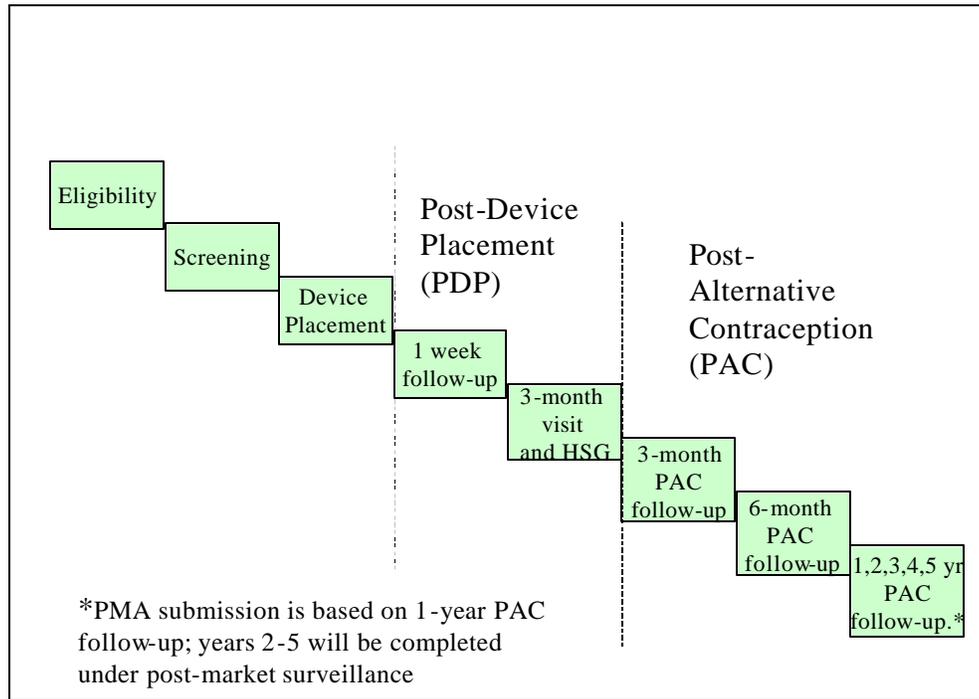
Protocol

Women in this study were followed at the following time points:

- ?? One week-post device placement (PDP)
- ?? 3-months PDP
- ?? 3, 6, and 12 months post-alternate contraception (PAC)

In addition, women will be followed at 18 months PAC and annually for five years under post-market surveillance.

This figure provides an overview of the clinical trial visits.



Placement Rates

Of the 507 women in the Device Evaluation Group, bilateral placement was achieved in 464 (92%), and single Micro-insert placement was achieved in the 2 women with a unicornuate uterus (100%). Of the 41 women (8%) with bilateral tubes who did not achieve bilateral placement, 15 (37%) were found to have proximal tubal occlusion (PTO) on follow-up HSG. Eliminating these women from the analysis of placement rates results in an overall bilateral placement rate of 464/492 (94%).

Satisfactory Micro-Insert Location/Occlusion Rates

A total of 456/464 women (98%) with bilateral placement completed the 3-month post-device placement visit and underwent an HSG. Of those 456 women, 437 (96%) were noted on HSG to have Micro-inserts in satisfactory location. Of those

437 women, 421 (96%) were also noted to have bilateral tubal occlusion. Nine of the 19 women with Micro-inserts in unsatisfactory location returned for a second placement procedure to replace an expelled Micro-insert. All achieved bilateral placement and were found on follow-up HSG to have bilateral occlusion and Micro-inserts in satisfactory location. All of the 16 women who had tubal patency at the initial HSG chose to undergo a second HSG 3 months later, and all were found to have bilateral occlusion on the second HSG. Therefore, of the 456 women with bilateral placement completing the 3-month visit, 446 (98%) were ultimately found to have Micro-inserts in satisfactory location and bilateral occlusion. In addition, 100% (446/446) of the women with Micro-inserts in satisfactory location ultimately had bilateral occlusion.

Reliance Rates

As stated above, 446/456 women (98%) with bilateral placement completing the 3-month PDP visit were able to rely on Essure for contraception. In addition, 3 women with bilateral placement did not have an HSG but chose to begin relying on Essure. Also, four women with unilateral placement and either confirmed contralateral PTO (2) or a unicornuate uterus (2) were able to rely on Essure for contraception. Therefore, among the 507 women in the Device Evaluation Group, 453 (89%) were ultimately able to rely on Essure for contraception, and among the women with bilateral placement, 449/464 (97%) were ultimately able to rely on Essure for contraception. These percentages are conservative since they count lost-to-follow-up women as “not relying”.

Adverse Event Rate

Adverse events on the day of the placement procedure were reported in 17 (3%) women. All events were resolved prior to the woman being discharged from the recovery room, except for one woman who required overnight observation following an adverse reaction to pain medication. Day of procedure adverse

events included the following, all of which occurred in <1% of cases: vomiting, vaso-vagal response, hypervolemia, band detachment, perforation, excessive vaginal bleeding, and “other” (skin itching, bloating, loss of appetite, and reaction to saline used for uterine cavity distension).

Adverse events that *initially* prevented the woman from relying on Essure occurred in 21 (4.5%) women. These were primarily Micro-insert expulsions following original Micro-insert placement that was out-of-specification. Nine of the women who experienced an expulsion chose to undergo a second placement procedure, and all were successful. Therefore, including the perforation that was diagnosed on the day of placement, adverse events that *ultimately* prevented reliance occurred in only 12 women (2.6%). The most frequently reported adverse events reported in the first year (fifteen months PDP) that did not prevent the woman from relying on Essure, but were rated by the Investigator as at least “possibly” related to Essure, were back pain (8.4%), and abdominal pain/cramps (3.4%). All other events occurred in less than 3% of women.

Patient Satisfaction/Comfort

Women in the study consistently rated their overall satisfaction and comfort in wearing the Micro-inserts as very high. One-week post-device placement, >95% of women rated their comfort as “good” to “excellent” and their satisfaction as “somewhat satisfied” to “very satisfied”. At all subsequent study visits, 99% of women rated their comfort with wearing Essure as “good” to “excellent”. At all study visits, at least 98% of women rated their overall satisfaction as somewhat to very satisfied (this included women who were not able to rely on Essure).

Pregnancy Prevention

There have been no pregnancies in any of the 453 women who have relied on Essure for contraception (449 with bilateral placement). There are 408 women

with bilateral placement who have been followed for at least one-year after relying on Essure for contraception and 14 women who began relying on Essure but subsequently were lost-to-follow-up (there are 3 additional women who were lost-to-follow-up prior to the 3-month PDP visit, at which women are told whether they can begin relying on Essure). The remaining 27 women with bilateral placement who are relying on Essure have completed from 7-11 months of follow-up.

There were 4 luteal phase pregnancies reported in the Pivotal trial (pregnancies occurring prior to Essure Micro-insert placement but not detected on the day of placement). None of these 4 women became pregnant while relying on Essure for contraception. Each of the pregnancies in these four women was terminated, and each of the four women was subsequently able to rely on Essure for contraception and has not reported a pregnancy while relying on Essure.

Combined with data from the Phase II study of Essure, this equates with over 627 women-years of first year effectiveness evaluation (and 272 woman-years of second year evaluation).²⁶ The current estimate of the one-year effectiveness rate based on these combined data is 99.84%.

Summary

In summary, we believe that the data contained in this Pivotal Trial Report, together with the data provided elsewhere in the PMA, provide a reasonable assurance of the safety and effectiveness of the Essure System based on valid scientific evidence.

²⁶ One woman in the Phase II trial who received a prior device design (Beta Design of the STOP Device) that was discontinued in 1998 became pregnant after relying on the discontinued design for 2 years. This pregnancy is not included in the Phase II effectiveness calculation since it is a different device than that for which approval is being sought. The device studied in the Pivotal trial is the Gamma version of the STOP device. The Gamma version has been trademarked as “Essure”. All prior versions are referred to as “STOP” with a version name: alpha or beta.