Essure Summary of Study Results extracted from PAS Study Status web page
for the two PAS ordered in conjunction with original PMA approval

1. Post-Approval Study (PAS) I: 5-year follow-up under Essure TM System Phase II and Pivotal Trials

General	
Application Number	P020014
Current Protocol Accepted	11/04/2002
Study Name	5 year follow up
Study Status	Completed
General Study Protocol Parameters	
Study Design	Prospective Cohort Study
Study involve follow-up of premarket cohort (Y/N)	Yes
Data Source	New Data Collection
Comparison Group	No Control
Analysis Type	Descriptive
Study Population	Transit. Adolescent B (as adults) : 18-21 yrs, Adult: >21
Detailed Study Protocol Parameters	
Study Design Description	Extended follow-up (5 years) of premarket study cohorts: The Phase II Study and the Pivotal Study (formerly known as STOP). The Phase II Study was a prospective, multi-center, international study of women seeking permanent birth control. There were sites in the US, Australia, Belgium, and Spain. The Pivotal Trial was designed as a multi-center, non-randomized, single-arm, international study of women seeking permanent contraception. The study was conducted in the U.S., Europe, and Australia.
Study Population Description	Adult women seeking permanent birth control. The study included participants of the premarket cohorts (Phase II and Pivotal Trial), ages 21 to 45 years old.
Sample Size	Phase II Study: 269 women enrolled Pivotal Trial: 657 women enrolled
Data Collection	Phase II Study: Study primary objectives were to evaluate: Essure micro-insert placement rate, woman's tolerance and recovery from the micro-insert procedure, safety of the micro-insert procedure, woman's tolerance of the implanted micro-inserts, long-term safety of the implanted micro-inserts, and

	effectiveness of the micro-inserts in preventing pregnancies. Pivotal Trial: Primary study endpoints: prevention of pregnancy, safety of the micro-insert placement procedure, and safety of the micro-insert wearing. Secondary endpoints included: participant satisfaction with the micro-insert placement procedure, participant satisfaction with micro-insert wearing, bilateral micro-insert placement rate; and development of a profile for an appropriate candidate for the Essure procedure.
Followup Visits and Length of Followup	For both studies, women were followed at: 1 week-post device placement (PDP), 3 months PDP, 3, 6, and 12 months post-alternate contraception (PAC); and yearly through 5 years, as part of the post-approval study.
Final Study Results	
Actual Number of Patients Enrolled	Phase II Study: 269 women enrolled, 227 underwent microinsert placement procedure. Remaining 42 women voluntarily withdrew, were excluded at screening or enrolled in Pivotal trial. 2 US sites(44 women), 1 site in Australia (130 women), 1 site in Belgium (28 women) and 1 site in Spain (25 women). Pivotal Trial: 657 women enrolled - 518 underwent the Essure procedure and 453 women achieved bilateral occlusion 3 months post-procedure (4 unilateral placements). 6 of the women were followed for safety only
Actual Number of Sites Enrolled	Phase II Study: 5 sites Pivotal Trial: 13 sites
Patient Follow-up Rate	Phase II Study: 86.3% at 1-year; 85.5% at 2-years; 80.2% at 3-years; 77.5% at 4-yeara; 75.3% at 5-years. Pivotal Trial: 97.5% at 1-year; 92.0% at 2-years; 89.4% at 3-years; 85.2 at 4-years; 81.6% at 5-years
Final Safety Findings	**Phase II Study:** Long-term Safety: Adverse events after the day of the procedure occurred in 9% of the women; 5% of these events were related to period pain, and ovulatory pain or changes in menstrual function. The other adverse events included: perforations (7), expulsion (1), unsatisfactory device location (1), and a retained micro-insert fragment (1). The perforations accounted for 3% of the patients that underwent the procedure. Four perforations were identified at the 3-month post-procedure evaluation; one was identified at the 18-month post-procedure evaluation. One additional case was of a peri-tubal perforation noted on gross examination following device removal due to pain. A seventh case was discovered when the woman had laparoscopic hysterectomy, the right device had perforated the tube. Six of the seven women that suffered perforations had the micro-insert located in the peritoneal cavity. In four of these women the device was removed successfully, in one woman the device was left in the peritoneal cavity. For the case of a retained micro-insert fragment, the event occurred during an attempt to remove the device that resulted in the broken distal ball tip. At the time of final report submission, there have been no reports of clinical sequelae for this case. **Pivotal Trial**: Adverse events that initially prevented reliance by

	the woman 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, adverse events that ultimately prevented reliance occurred in only 12 women (2.6%). The most frequently reported adverse events reported in the first year 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 (6.2/1000 women-months), abdominal pain/cramps (2.6/1000) and dyspareunia (2.5/1000 women-months). All other events occurred at less than 2.5/1000 women-months of wearing.
Final Effectiveness Findings	In both studies, no pregnancies were reported while relying on Essure for contraception.
Study Strengths and Weaknesses	The studies were limited in that there were no comparison groups. Both were designed to provide the pregnancy rate with the precision around it (95% Confidence Interval). Another limitation is the length of follow-up. Both studies were designed to provide an estimate of pregnancy rate out to 5 years; after which point there is no precise data on effectiveness and safety of the device, from these two studies. One of the strengths of the studies is the observed follow-up rates. The study provides a precise estimate of the pregnancy rate at 5 years
Recommendations for Labeling Changes	Yes, label was updated to include the 5-year performance data

5 year follow up Schedule

Report Schedule	Report Date Due	FDA Receipt Date	Reporting Status
Final Report	04/01/2008	04/01/2008	On Time

2. Post-Approval Study (PAS) II: U.S. Post-Approval Study for Newly Trained Physicians

General	
Application Number	P020014
Current Protocol Accepted	11/04/2002
Study Name	Newly Trained Physicians
Study Status	Completed
General Study Protocol Parameters	
Study Design	Cross-Sectional Study
Study involve follow-up of premarket cohort (Y/N)	No
Data Source	New Data Collection
Comparison Group	Historical Control
Analysis Type	Analytical

Study Population	Transit. Adolescent B (as adults) : 18-21 yrs, Adult: >21
Detailed Study Protocol Parameters	
Study Design Description	This study was designed to document the bilateral placement rate at first attempt for newly trained physicians in the U.S. These data were used to evaluate the training procedures and to update labeling.
Study Population Description	Study population as per device indication . This device is indicated for permanent birth control (female sterilization) by bilateral occlusion of the fallopian tubes in adult women seeking permanent birth control.
Sample Size	The study was originally designed to enroll 800 women from 40 physicians in the commercial setting.
Data Collection	Data collected included: (1) successful bilateral placement rate at first attempt, and (2) identification of factors predictive of failure to achieve bilateral placement at first attempt.
Followup Visits and Length of Followup	No patient follow-up was conducted as part of this study, with the exception of the follow-up data of the HSGs performed to evaluate the reasons for placement failure in women who desired a second attempt of device placement.
Final Study Results	
Actual Number of Patients Enrolled	After reviewing the final report, the Agency considered the conditions of approval for this study to be satisfied, with 514 women enrolled.
Actual Number of Sites Enrolled	39
Patient Followup Rate	N/A
Final Safety Findings	Safety: There were 38 malfunctions in 27 cases, in 9 the distal tip was bent, the sponsor does not consider these are malfunctions. There were no reports of adverse events related to bent tips. There were 29 device malfunctions that included detachment problems, deployment issues, thumbwheel retraction difficulty, inner sleeve detachment and failure of delivery catheter to retract. Placement rate: There were 13 adverse events that included perforation, pelvic pain, bleeding, light headed, increased blood pressure and temporary decreased pulse. There were 476 women in whom bilateral placement was possible. After excluding all confounding, bilateral placement was achieved in 458 women for 96.2% (458/476) success rate. Bilateral failure happened in 10 women for 2.1% failure rate (10/476). After original approval of Essure system a new coil catheter was approved. The sponsor did a comparison of success rate by design. After excluding all confounding there were 184 procedures with the original model (gamma) and 297 procedures with the new model (coil catheter design). The new model performed better than the old, with a 96.0% success rate for the new coil catheter and 94.0% for the gamma model. Additionally, bilateral failure was less frequent with the new model (1.3% vs. 3.3%). The gamma model was discontinued in September 2003.
Study Strengths and Weaknesses	Study provided precise estimate of bilateral placement at first attempt among newly trained physicians. Although the sponsor did not enroll the required number of women as per protocol, they were able to demonstrate with Bayesian statistics, that the

	observed rate was not different from the rate observed in experienced physicians.
Recommendations for Labeling Changes	Update label to include results from the PAS (bilaeral placement rate from newly trained physicians). Labeling should include the information on the number of patients excluded and why these patients were excluded from the post-approval study.

Newly Trained Physicians Schedule

Report Schedule	Report Date Due	FDA Receipt Date	Reporting Status
Final Report	03/16/2005	03/16/2005	On Time
Final Report amended	07/05/2005	07/05/2005	On Time