The Controversy Over Essure Birth Control

Sydney Sheffield
Tulane University, New Orleans, Louisiana, USA

Abstract: When the Food and Drug Administration approved Essure for market release in 2002, the medical community held its breath. Essure was a revolutionary, non-surgical form of women's permanent birth control that could be implanted in 20 minutes with only two days of recovery time. Further, the Essure device boasted the ability to make sterilization accessible to women who are unable to undergo surgery. In the years after the device's approval, a percentage of women began vocalizing adverse health effects they had experienced after having the device implanted. By 2018, the Facebook support group called "Essure Problems" had accumulated over 40,000 members. This case investigates the intricacies of the FDA's premarket approval process for medical devices, Essure's journey through premarket approval and its time on the market, and the FDA's responsibility to promote public health without stifling medical innovation. Ultimately, the FDA faced the dilemma of responding to the real and vocal concerns of the "Essure Problems" women considering clinical evidence and informed consent. After the FDA first attempted to ameliorate the issue by introducing a patient decision checklist and a black box warning, Bayer decided to discontinue sales of Essure in 2018, citing a decline in sales. Despite the inadequacies of the current FDA medical device approval process revealed in this case, the FDA continues to allow potentially dangerous medical devices to enter the market. Women throughout history have found strength in numbers when faced with injustice, a trend that is evolving and expanding with the growing accessibility of social media.

Elena Mendez's Story[1]

In 2008, Elena Mendez made an appointment with her obstetrician-gynecologist because of a recent onset of heavy menstrual bleeding. The bleeding had been so severe that Mendez had difficulty leaving her home for days at a time. At the appointment, she was diagnosed with uterine fibroids, a common condition for women of childbearing age that is characterized by benign tissue growths in the uterus. Her doctor recommended she undergo an endometrial ablation—a procedure that destroys the superficial layer of the uterine lining—to remove the fibroids. But, as a condition of undergoing the ablation, she would need to also undergo a sterilization procedure, due to the increased risk of miscarriage and ectopic pregnancy if fertilization of an egg were to occur after the ablation. Her OB-GYN recommended a fairly new form of permanent birth control called Essure, which would not require surgery, could be implanted in 45 minutes, and would allow Mendez to forego the one to three-week recovery time usually associated with sterilization, so she could immediately return to work. Essure consists of two coils made of metal that are inserted into

[1] All information regarding Elena Mendez obtained from a video call interview with Elena Mendez on November 3, 2018.

the fallopian tubes. Mendez knew that she was allergic to nickel after having rejected three nickel piercings, so she alerted her doctor of her allergy. He assured her that her nickel allergy would not be a problem with the Essure device. After some thought, Mendez agreed to both procedures and underwent an endometrial ablation and permanent sterilization at 37 years old. "Right afterward, I didn't feel right, but I couldn't put my finger on it. I just was feeling very tired… Then, all of a sudden, the pelvic pain was horrific. Horrific," Mendez recalled of the day after her procedure.

The excruciating pelvic pain was only the beginning of a slew of side effects Mendez endured over the next six and a half years. She felt perpetually fatigued and woke up several mornings every week with rashes covering her abdomen, arms, and hands. She reported inexplicable weight gain, constant general discomfort, joint pain, and hair loss. She underwent multiple dental surgeries after 2008 due to inflammation of her gums, despite having had no dental issues prior to the Essure implantation. In addition to the physical repercussions, the constant pain took a toll on Mendez's personal and marital relationships, and she struggled at work. At the emergency room where she worked as a nurse, she was "walking around holding [her] own pelvic area looking like [she] needed an emergency room bed."

Initially, Mendez did not attribute these symptoms to her birth control. She consulted many different doctors over the next several years, ranging from endocrinologists to other OB-GYNs. Each told her the same thing: "They kept telling me, you know, 'nothing's wrong.' What do you mean nothing's wrong? I can't get out of bed, I can't have sex, my pelvis is killing me, my back is killing me."

In 2013, after her medical consultations proved futile in explaining the array of health effects she had been experiencing, Mendez turned to "Dr. Google". Upon entering her major symptoms into the search bar, Essure appeared as the top result. With further searching, Mendez found and joined the Facebook group titled Essure Problems, which connected her with approximately 41,000 other women experiencing symptoms akin to her own after having chosen the Essure permanent birth control device themselves.

The Medical Device Approval Process

The US Food and Drug Administration is the governing entity charged with regulating all products that come in contact with the human body, including drugs, biological products, cosmetics, human and animal food, and—since 1976—medical devices (FDAa n.d.). In 1976, Congress passed the Medical Device Amendments Act. This legislation placed the regulation of medical devices under the FDA's jurisdiction, created a system for classifying devices based on risk, established the processes of premarket approval (PMA) and 510(k) clearance, cleared all pre-amendment devices for the market without further consideration, and established many post-market requirements for medical devices (FDA 2017). As such, the FDA is responsible for the approval of medical devices to enter the American market, as well as the monitoring and possible recall of devices post-market.

The classification system created by the Medical Devices Amendment Act consists of three classes and delineates which of the two available processes a device is required to undergo before it can be released to the market. All three classes are subjected to general controls, including "establishment registration, device listing, premarket notification, and good manufacturing practice requirements," however, market clearance of Class II and Class III devices are further constrained by specialized controls and PMA, respectively (Johnson 2016, 5).

Low-risk devices that are "substantially equivalent" to a previously-existing device, or predicate device, fall under Classes I and II, allowing them to bypass the more stringent PMA

process and follow the 510(k) pathway (FDA 2017, n.p.). The 510(k)-clearance process entails submitting an application to the FDA at least 90 days prior to marketing a device, which demonstrates that the device in question is substantially equivalent to a predicate device. Class I devices are those that do not "present an unreasonable risk of illness or injury" and are also not intended for use in sustaining human life, such as elastic bandages or examination gloves (National Academies Press 2011; FDA 2012). Class II medical devices, like powered wheelchairs and some pregnancy test kits, present a moderate level of risk and require specialized controls within the 510(k) clearance process to assure safety and effectiveness. Such special controls may include "special labeling requirements, mandatory performance standards, and postmarket surveillance" (Johnson 2016, 6). The FDA approves 98% of the devices submitted via the 510(k) clearance (Johnson 2016). According to the FDA, 47% of all medical devices cleared for the market are Class I devices, while 43% are Class II, making up a total of 90% of the medical device market (FDA 2017).

Class III medical devices—like pacemakers, breast implants, and the Essure birth control device—comprise the remaining 10% of devices on the market today. This classification is generally reserved for devices that present a "potentially unreasonable risk of injury or illness," "support or sustain human life," are of "substantial importance in preventing impairment of human health," are not substantially equivalent to an existing device, or otherwise cannot be classified as Class I or Class II. These devices are regulated by the PMA process, which requires reasonable assurance that the device is safe and effective for its intended use through collection and analysis of scientific evidence (FDAa n.d., n.p.). A PMA application must include the following: summaries of nonclinical and clinical data, a device description, indications for use of the device, a description of the marketing history of the device, proposed labeling, and a description of the manufacturing process (Johnson 2016). After an application is filed, FDA regulations allow 180 days for the appropriate advisory committee to review the PMA application and determine whether the device should be approved for market release (FDAa n.d.).

The PMA process has long been criticized within the medical and political communities alike for failing to provide sufficient assurance of the safety and effectiveness of high-risk medical devices (Johnson 2016; US Institute of Medicine 2011). Notably, the device industry's motivations for increases in revenue and producing innovative new products conflicts with the public health precautionary principle, which espouses erring on the side of caution in the interest of public safety (Martuzzi and Tickner 2004). This conflict places the burden of balancing conflicting interests on the FDA. The FDA is charged with weighing the benefits of releasing a new, potentially lifesaving device to market against the potential health risks using the PMA process, which has often been considered insufficient.

Researchers involved in one 2009 study on cardiovascular devices approved via the PMA process concluded that "premarket approval of cardiovascular devices by the FDA is often based on studies that lack adequate strength and may be prone to bias" (Dhruva, Bero, and Redberg 2009, 2679). This study found that 65% of the 78 devices studied were approved based on a single study, and only 52% of the 123 studies associated with these devices were controlled (Dhruva, Bero, and Redberg 2009). By contrast, FDA approval of drug applications requires a minimum of two randomized and controlled trials (Johnson 2016). The researchers in this study reason that FDA regulation of medical devices may be less strict than for drugs due to the FDA having less experience with the approval of devices in comparison to drugs, however "the bar for evidence of benefit should be higher for devices because they are implanted and cannot simply be discontinued, as drugs can" (Dhruva, Bero, and Redberg 2009, 2684). Another study that surveyed stakeholders

in the medical device industry—including industry experts, healthcare practitioners, and industry regulators—found that 56% of the stakeholders felt that "medical device regulation is inconsistent and unpredictable" and 50% felt that the "FDA should increase collaboration with academia and industry" (Teow and Siegel 2013, 2).

The report for a 2010 medical device approval workshop hosted by the Institute of Medicine of the National Academies summarized director of the nonprofit Medical Device Safety Institute William Maisel's view on the issue:

> A difference between devices and drugs… is that conducting a 4-year randomized trial of a device would essentially be holding back the advancement of technology. Our goal and our measurement… should be benefit to public health. That means coming up with a total-product approach that balances the risk posed by bringing a product to market and the need to obtain information. For many devices, a clinical study is necessary to understand the final benefit-risk ratios and identify problems that might arise in a particular patient population. But for the technology itself, most information can be obtained better at the bench than in large clinical trials (Wizemann 2011, 42).

Maisel asserts here that the current PMA process is sufficient for some devices because much of the critical information regarding the technology of the device is best tested within the lab. He argues devices should be released to market earlier rather than later in order to promote advancement of technology, as long as the proper clinical studies and lab studies have been conducted.

Essure's Pre-Market Approval Journey

In 1987, a physician named Amy Thurmond and a medical entrepreneur named Julian Nikolchev met at a conference held by the Radiological Society of North America. At this conference, Thurmond presented data from her recent study regarding the treatment of infertility by unblocking fallopian tubes with a catheter. Inspired, Nikolchev approached Thurmond after her presentation with an idea that would revolutionize permanent birth control: if unblocking fallopian tubes could encourage fertility, then non-surgically placing a device in the fallopian tubes could conceivably prevent conception (Block 2017).

By 1988, Nikolchev and Thurmond had developed a prototype to test their idea. The prototype consisted of a steel outer coil attached to a steel inner coil wrapped in polyethylene terephthalate (PET). Initial experimentation of the device on 37 rabbits yielded a 100% contraception rate for the rabbits whose devices remained properly implanted in their fallopian tubes (Thurmond et al. 2004). Based on this study, the FDA approved the device for use in clinical trials. Nikolchev later raised $35 million of venture capital and founded the company Conceptus, Incorporated to manufacture, market, and test his new device (Block 2017). He called it Essure.

For the human clinical trials that followed, Conceptus modified the Essure device by changing the material used for the outer coils from steel to a recently-developed nickel-titanium elastic alloy called Nitinol. Use of this alloy allowed the coils to be tightly packed into a delivery catheter for insertion and then also to expand to conform to the shape of the fallopian tubes after insertion (Block 2017). Upon expansion, the PET fibers of the inner coil would "elicit an intended

benign, occlusive tissue response, resulting in tissue in-growth into the device that anchors the device and occludes the fallopian tube."[2] (FDAb n.d., 1).

Between November 1998 and June 2001, Conceptus conducted two clinical studies to evaluate the safety and effectiveness of the Essure device in preparation for Essure's PMA application. The Phase II study tracked 206 women after successful insertion[3] of at least one Essure coil, and the Pivotal study tracked 476 women with the same criteria, for a total of 682 women studied. All of the participants were between the ages of 21 and 45 years of age, had been seeking permanent birth control, had undergone at least one live birth, and had regular menstrual cycles. One year after implantation of the Essure device, 3.8% of the women in the Pivotal study reported abdominal pain and cramps, 9.0% reported back pain, 2.5% reported headaches, 2.5% reported severe pelvic or lower abdominal pain, and 2.9% reported general pain or discomfort. In the Phase II trial, 5.8%[4] of the women with at least one coil successfully inserted reported episodes of "period pain, ovulatory pain, or changes in menstrual function." Of the 632 women for whom bilateral insertion of the Essure coils had been successful, all were tracked for at least one year. Thirty-one percent of these women were tracked for two years, and 0.05% were tracked for three years. After one year, the study yielded an effectiveness rate[5] of 100% among the 632 women. After two years, the trials again showed a 100% effectiveness rate among the 197 women who were still being monitored. Data regarding the risks and effectiveness of the Essure device beyond two years after insertion was not available at the time the PMA application was submitted, however the application promised that "data for up to 5 years of wear will become available as participants in the clinical trials of safety and effectiveness continue to be followed" (FDAb n.d., 4).

On November 4, 2002, the FDA determined that Essure demonstrated a reasonable assurance of safety and effectiveness and approved Essure as a Class III device via expedited review within the PMA process. As a condition for this expedited approval, the FDA mandated two post-approval studies to first gather data on the original participants of in the Phase II and Pivotal trials after five years of using Essure, and second, evaluate the success rate for bilateral placement of the Essure device among newly-trained physicians (FDA 2018).

Essure on the Market

The Essure device was embraced by the public and the medical community alike. Upon its market approval, Essure became the first permanent sterilization alternative to surgery. Essure is a less invasive and less time-consuming procedure than surgery; according to Essure's PMA application, the implantation of the Essure device should not exceed 20 minutes and women should be able to return to normal activity within two days of implantation (FDAb n.d.).

The Centers for Disease Control (CDC) analyzed national data and individual medical records to estimate that approximately four deaths occur per 100,000 surgical tubal sterilizations (Peterson et al. 1982). According to one study of 9,475 women from 1978 to 1987, which tracked women up to one year after their surgery, tubal occlusion via surgery has a major complication

[2] See Appendix A for ideal Essure insertion

[3] Successful insertion is determined when patients return three months after the initial procedure for the transvaginal ultrasound/hysterosalpingogram confirmation test that ensures both proper placement of the Essure coils and sufficient occlusion of the fallopian tubes (FDAb; FDAc).

[4] The percentages of adverse health events calculated for both trials reflect the number of events reported as the numerator and the number of women in the trial as the denominator. Therefore, even if a single woman reported several instances of the same adverse health event, she is only included in the denominator once. As such, these percentages may "over-represent the percentage of women who have experienced the health event" (FDAb n.d., n.p.).

[5] Effectiveness rate here refers to the percentage of women who relied solely on the Essure device as a contraceptive and did not become pregnant.

rate of 1.6%, which includes reports of bleeding, rehospitalization, unintended surgery, fever, and other life-threatening events (Jamieson et al. 2000). While the rate of adverse health events in Essure's clinical trials exceeds 1.6%, the health events reported with Essure were not life-threatening; the results of the clinical trials yielded no deaths and only eight of the medical device reports, or 0.0003%, related to death of the patient (FDAb n.d.). Another study of 105,357 women that investigated the clinical risks of Essure in comparison to laparoscopic sterilization—a method of tubal ligation—concluded that use of Essure is associated with a higher risk of bodily complication than laparoscopic sterilization, but a lower immediate risk of procedural complications than laparoscopic sterilization (Bouillon et al. 2018). Dr. Elizabeth Deans, a practicing OB-GYN at Duke Health and the Veterans Affairs hospital in Durham, North Carolina, has first-hand experience with Essure's benefits:

> I had a patient who is too sick to get surgery. She's too sick to be pregnant, and she has a cardiac issue. She's using contraception, but she says she wants to be responsible and get sterilized. If she can't get general anesthesia, I really need to do a laparotomy or a mini-laparotomy which is a bigger procedure than Essure. Essure is a great option for many women who are not great surgical candidates (E. Deans, personal communication, November 11, 2018).

Doctors, too, benefitted from the new device. Inserting an Essure device in a patient required much less time and preparation than performing a surgical tubal ligation. Additionally, Conceptus estimates that a doctor could earn more than $1,100 in insurance reimbursements for every Essure device inserted, which is $590 more than the $510 a doctor earns for every surgical sterilization (Block 2017). The higher reimbursement rate is meant to "cover office overhead and the equipment necessary to insert Essure," though it does also indirectly offer an incentive for doctors to recommend Essure over surgical alternatives (Block 2017, n.p.).

As of December 31, 2017, the FDA received 26,773 medical device reports related to Essure. These reports include 21,215 reports (79.2%) about abdominal pain, 9,846 reports (36.8%) about menstrual irregularities, 7,231 reports (27.0%) about headaches, and 4,970 reports (18.6%) about weight fluctuations. Additionally, the FDA received 1,826 reports of pregnancies in patients who received the Essure implant within the same time period (FDA 2018).

As agreed upon, Conceptus conducted two post-approval studies. The first study, which evaluated adverse health events in the group of women studied in the original clinical trials, found that no pregnancies had been reported by any of the women remaining in the program—which comprised 70% of the original group—as of April 1, 2008, 9% of women within the Phase II trial group reported adverse events in the years following implantation of Essure; 5% of the reports were related to "period pain, and ovulatory pain or changes in menstrual function," and 3% of the reports were related to perforation of nearby tissue. The second study, which evaluated the bilateral placement rate for newly trained physicians, found that bilateral placement was successful in 458 out of 476, or 96.2% of women studied. In the wake of this bilateral placement study, a PMA supplement for a new coil catheter was approved for the Essure system, which yielded a higher success rate than the original "gamma model" (FDA 2018., n.p.).

Sanket Dhruva, a cardiologist at Yale University and researcher of medical devices, believes that, even with the post-approval studies, the clinical trials for Essure were insufficient to assure safety and effectiveness. In an interview with Jennifer Block from the Washington Post, he argued that "Ideally…the researchers would have given 1,000 women Essure and another 1,000

women laparoscopic sterilization and followed them for five years to compare rates of pregnancy, complications, hysterectomy and repeat surgeries" (Block 2017, n.p.). Though, with the potential to provide women across the world with a nonsurgical alternative for sterilization, neither Conceptus nor the FDA mandated the thorough testing Dhruva describes.

In 2013, the billion-dollar pharmaceutical company, Bayer AG, bought Conceptus for $1.1 billion. To date, Bayer estimates that over 750,000 Essure devices have been sold worldwide (Bayer 2018c).

Essure Problems

In 2009, just a few miles away from and one year after Elena Mendez's Essure implantation, Angie Firmalino[6] from Tannersville, New York underwent the Essure procedure as well. After giving birth to two children and raising four children in total, Firmalino desired a permanent form of birth control. When the on-call surgeon who performed her C-section during the birth of her youngest child failed to follow her previously-stated wishes to simultaneously undergo a tubal ligation, she turned to her OB-GYN who persuaded her to opt for Essure. Firmalino did not receive a call from her OB-GYN's office to schedule her three-month confirmation test until six months after her procedure, at which point she was informed that the physician only did confirmation exams at 7AM. As a mother of four children—including a nine-month-old infant at the time—who lived an hour away from the facility, Firmalino could not make any such appointments. The medical assistant on the phone assured her it would not matter— "Well, it's the only time they do this type of appointment, but at six months you should be fully occluded anyway… so don't worry about it." Firmalino's Essure coils were never checked for proper placement or sufficient occlusion.

In the two years after her procedure, Firmalino faced debilitating symptoms including "sharp stabbing pain in my lower left side, back pain, heavy and constant bleeding, joint pains, fevers, fatigue, and depression." When she visited her OB-GYN in early 2011 for a routine exam and confided in the nurse-midwife about her symptoms, the nurse scheduled Firmalino for an ultrasound, and the screen showed that one of the coils had migrated to Firmalino's uterus, just as Mendez's had three years prior.

On April 20, 2011, after searching out a new OB-GYN, Firmalino underwent a surgical procedure to remove both of her Essure coils and ligate her fallopian tubes. Immediately after the procedure, the stabbing pain in Firmalino's side disappeared and her period had returned to normal, however the fatigue, joint pain, back pain, and recent onset headaches persisted. Months later, Firmalino's localized pain and menstrual irregularities returned. Around the same time, Firmalino was learning more online about the possible outcomes of Essure device removal, which included fragmentation of the coils and subsequent inflammation. When she revisited the second OB-GYN, she expressed the concern that fragments of her Essure coil may have remained in her uterus, causing sequential pain, but the OB-GYN was not receptive—"She couldn't get me out of the door fast enough, she wouldn't even *look* at the information I had brought to her and told me she had gotten it *all* out" (Firmalino 2016, n.p.). Firmalino finally went to her primary care physician who ordered a pelvic x-ray, revealing several foreign bodies in Firmalino's pelvis. On March 14, 2014, Firmalino wrote on her Essure Problems website blog:

> I've had enough. My body is deteriorating. I weigh 107 pounds. I get sick all of the time, I have no energy, no strength, and it hurts to eat food. It feels like I am 100

[6] All information regarding Angie Firmalino obtained from Firmalino's blog (Firmalino 2016).

> years old. I just want my life back, my health back. I want to be able to play with my four year old [sic] son. He's never known a healthy mother. My poor husband doesn't have the wife he married. It hurts to have sex which has put a huge strain on our marriage. I feel hopeless (Firmalino 2016, n.p.).

Firmalino spent the next year of her life in and out of the operating room for medical issues she attributes to Essure. She underwent one shoulder surgery, one elbow surgery, a complete hysterectomy, two follow-up surgeries to repair tears in the sub-mucosal layer of her uterus, two rounds of antibiotics for a subsequent infection, and ten months of biweekly silver nitrate treatments to remedy the near constant bleeding. Firmalino's various specialists have diagnosed her with cervical facet syndrome, occipital neuralgia, bursitis, tendonitis, tendinosis, and epicondylitis.

In 2011, in an effort to warn her friends and family members who may be considering permanent birth control in the future and share the extent of her experiences with Essure, Firmalino created the Essure Problems Facebook group. What began as a small community of Firmalino's supporters grew to become a national forum for women across the country to post about their negative experiences with the Essure device, find guidance and support from women with similar experiences, and mobilize against the manufacturing and marketing of Essure in the US. "I was blown away to find so many women joining and telling similar stories, awful stories," Firmalino says.

Today, the Essure Problems group contains 40,905 members. Over the past seven years, 17 women have assumed the roles of administrators for the group, acting as leaders and spokeswomen in the campaign to remove Essure from the market and providing a support system for women impacted by the device. After Mendez joined the Essure Problems group in 2013, she slowly became more and more active in the online community. In 2015, Firmalino and other administrators reached out to Mendez and invited her to join the administrative team. Since then, Firmalino, Mendez, the other Essure Problems administrators, and women around the country have launched a grassroots movement against Bayer and the Essure device (E. Mendez, personal communication, November 3, 2018).

Essure Problems vs. Bayer

In 2012, Essure Problems administrators began contacting the FDA asking for meetings to discuss the growing number of reported adverse health events related to Essure. As more and more women had joined the Essure Problems Facebook group, trends of symptoms and injustices within the healthcare delivery system became apparent. Administrators further investigated the device, revealing a number of troubling facts. They discovered that the Senior Vice President of Clinical Research and Regulatory Affairs at Conceptus from 1994 to 2003, Cindy Domecus, served on the Center for Devices' OB-GYN Devices Advisory Board[7] that recommended the FDA approve Essure. Furthermore, the presence of nickel in the Essure device had not been disclosed to a vast number of women who had shared their experiences in the Essure Problems group, resulting in high rates of allergic reactions (Block 2017).

In 2011, a research group, unaffiliated with both Bayer and the FDA, analyzed the adverse events related to nickel allergy in patients with Essure implants and concluded that "the reported

[7] Industry representatives, like Domecus, are not permitted to participate in the vote to recommend or not recommend a device for FDA PMA, but some believe sitting on the panel allows representatives to influence the vote by interacting and building relationships with voting panel members (Block 2017; FDAa n.d.).

incidence of adverse events possibly related to nickel hypersensitivity in patients with Essure micro-inserts is extremely small (.04/1000)" (Zurawin and Zurawin 2011, S4). Consequently, the FDA approved the removal of nickel sensitivity as a contraindication for Essure. Now, with nickel sensitivity downgraded from a contraindication to a warning, the FDA does not require that physicians screen patients for such a characteristic, which explains Mendez's OB-GYN's assurance that her nickel allergy would not be a problem (Block 2017). It is unclear why Mendez and other women have reported allergic reactions following their implantations with Essure, considering the study's findings. But, as explained on *Reveal*'s podcast, "Her Own Devices: Is a Contraceptive Implant making us Sick?" the nitinol contained in Essure coils is only safe for use in medical devices due to treatment of the surface to trap the toxic nickel inside. Medical device engineer "Roger" commented on the podcast that "if there's a wear point, if there's a fracture, if you've got sharp edges that could propagate a fracture, there's all these potential failure modes" (Reveal 2017, n.p.). Based on Reveal's investigations, neither the FDA nor Bayer performed any fatigue testing on the device to determine whether years of use could expose the nickel.

When the FDA agreed to hold a public hearing in 2015 before the Center for Devices' OB-GYN Devices Advisory Board—the same panel which had recommended Essure's PMA in 2002—Essure Problems administrators marshaled 22 women from the Essure Problems group to testify about the negative impact the Essure device has had on their health and wellbeing. On September 24, 2015, the FDA, the OB-GYN Devices Advisory Board, and the 22 representatives from Essure Problems convened at the FDA's campus in Silver Spring, Maryland to "discuss currently available scientific data pertaining to Essure's safety and effectiveness, hear expert scientific and clinical opinions on the risks and benefits of the device, [and] hear concerns and experiences of women implanted with Essure" (FDA 2018, n.p.). At the meeting, Essure Problems women called for the FDA to pull Essure from the market.

In the wake of the 2015 public hearing, the FDA implemented an updated physician and patient label to include a black box warning and Patient Decision Checklist[8] (FDA 2018). According to the FDA, a boxed warning or black box warning "appears on a prescription drug's label and is designed to call attention to serious or life-threatening risks" (FDA 2012, 1). Under the Patient Decision Checklist provision, the FDA mandated that physicians provide a document for the patient to initial and sign, detailing the requirements for Essure placement, the pregnancy risks, what to expect after the procedure, and long-term risks (FDA 2018). Additionally, the FDA ordered Bayer to conduct another clinical trial using a control group, a factor which had been absent from previously conducted clinical trials on Essure. The results of this study are due in 2023 (Block 2017).

While the black box warning and the patient decision checklist signaled progress in assuring informed consent for women opting into the Essure implantation, the representatives from Essure Problems remained unsatisfied. In May 2017, several of these representatives continued to fight for pulling Essure off the market by rallying support on Capitol Hill for the 2017 Medical Device Safety Act, which would eliminate the 2008 Supreme Court ruling which protected manufacturers of Class III medical devices from lawsuits (Block 2017).

Despite the volume of adverse health event reports and the passion exhibited by women who had been negatively impacted by the Essure device, the medical community still largely supported the use of Essure. According to Jennifer Block's article, "The Battle Over Essure":

[8] See Appendix B for an example.

> The American Congress of Obstetricians and Gynecologists opposes the black box warning, citing a lack of "good, solid data," as Levy puts it. Planned Parenthood, which spoke in favor of the device remaining an option at the 2015 hearing, still offers Essure at 18 affiliates. And many physicians and researchers, as well as the Center for Devices' OB/GYN panel and Bayer, say Essure should stay on the market while further studies about its effects are conducted, because of the risks posed by the surgical alternative. Health-care watchdogs counter that there are other options available, such as IUDs, as well as vasectomy, which does not pose the same surgical risks as tubal ligation. For its part, the FDA told me that it "continues to believe Essure is safe and effective for many women — but also that some women experience very serious and sometimes debilitating problems (Block 2017, n.p.).

Should the FDA submit to the push from the Essure Problems movement to pull Essure off the market, despite its niche role in the permanent birth control market as well as the black box warning and patient decision checklist that assure informed consent? Should public outcry play a role in the FDA's decision-making even if the majority of women have not experienced negative health effects with Essure? Should the responsibility of a patient's safety transfer from the company to the patient if the patient is properly informed of all the associated risks? And what does "properly informed" mean?

Epilogue

On July 29, 2017, *Reveal*, a public radio program run by The Center for Investigative Reporting, produced a podcast on the story of Essure's creation and time on the market called "Her Own Devices: Is a Contraceptive Implant making us Sick?" On July 27, 2018, Netflix released the original documentary *The Bleeding Edge*, which featured Angie Firmalino, the Essure Problems Facebook page, and other women negatively impacted by the Essure device. In her review for The Guardian, Amanda Holpuch describes *The Bleeding Edge* as "a stark warning that a nightmare has been lurking in the medical industry for decades and it might be in your body" (Holpuch 2018, n.p.). Both pieces of journalism launched the controversy over the Essure device into public consciousness. In response, Bayer published a press release titled "Bayer Fact Checks Netflix's The Bleeding Edge" arguing that "the film presents an inaccurate and misleading picture of Essure by relying almost entirely on anecdotes, cherry-picking information to fit a predetermined conclusion, ignoring the full body of scientific evidence that supports the Food and Drug Administration's (FDA) determination that Essure's benefits outweigh its risks and disregarding the appropriate warnings that accompany the device." (Bayer 2018b, n.p.). Nevertheless, according to a press release from FDA Commissioner Scott Gotlieb, sales of Essure declined by 70% following the FDA's addition of the black box warning and Patient Decision Checklist to Essure labeling (Gottlieb 2018).

On June 20, 2018, Bayer announced plans to discontinue sales of Essure after December 31, 2018, citing a national decrease in demand (Gottlieb 2018). In tandem, Bayer published "An Open Letter to Patients and Providers About Essure," asserting that "our decision was not based on concerns about the safety and efficacy of Essure. Essure has been on the market for more than 15 years and has been successfully used by hundreds of thousands of women" (Bayer 2018a, n.p.). Bayer also noted in the press release that "the concerns raised about Essure are based primarily on

anecdotal reports from individual patients… however, anecdotal reports have limitations" (Bayer 2018a, n.p.).

In response, Dr. Deans, who earlier provided an example of one of her patients who had benefitted from the availability of Essure, said, "I think it's important that women have choices. I am very saddened that they're taking this away. What it means is that we have less options for women" (E. Deans, personal communication, November 11, 2018).

In the years since removal of her Essure coils, Elena Mendez has continued to exhibit adverse health effects; the fatigue, weight gain, and joint pain which began after implantation of the Essure device have persisted. Mendez notes that one positive from the whole process has been meeting empowering and wonderful women—"you can't believe how close you can become with someone you have never met in your life; that's why we say E-sister…who else could understand what we were going through" (E. Mendez, personal communication, November 3, 2018).

The FDA's system for approving medical devices remains unchanged, allowing future potentially harmful devices like Essure to make it to market. As technological innovation continues to characterize the 21st century, either the American public must adopt a more critical mindset toward those devices approved by the FDA or the FDA must revise their current approval process to ensure approved devices are held to the same safety standards as approved drugs. Meanwhile, patients remain the last line of defense as sentinels for their health and wellbeing. In the field of women's health, this means listening to and believing one another when health care professionals fail to, connecting with one another over shared experiences, and using our strength in numbers to bolster our voices.

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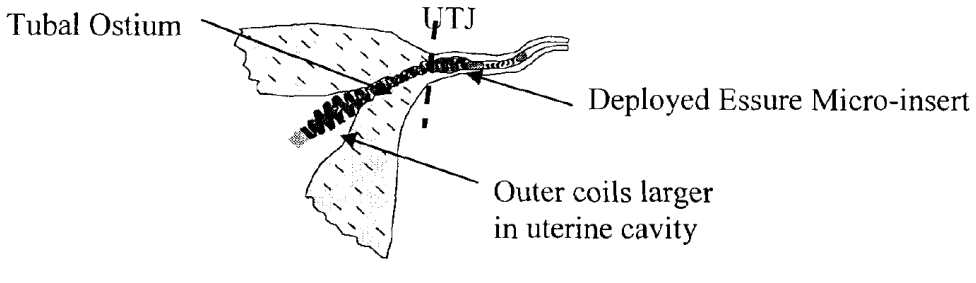
Appendix A: Excerpts from Essure PMA, Including Clinical Trials Results (FDAb n.d.)

Diagram III.1: Ideal Essure Micro-insert Placement



Appendix A (continued)

VIII. ADVERSE EVENTS

A. Patient Population

Between November of 1998 and June of 2001, a total of 745 women underwent an Essure placement procedure in two separate clinical investigations to evaluate the safety and effectiveness of the **Essure System** (227 in the Phase II study and 518 women in the Pivotal trial[1]). Some women underwent more than one procedure if successful bilateral placement was not achieved in the initial procedure. Placement of at least one Essure Micro-insert was achieved in 682 women (206 in the Phase II study and 476 in the Pivotal trial).

B. Observed Adverse Events

Tables 1 and 2 below present adverse events that prevented reliance on **Essure** for contraception in the Phase II and Pivotal studies, respectively.

Table 1
Phase II Study
Adverse events that prevented reliance on Essure for contraception

Event	Number	Percent
Perforation	6/206	2.9%
Expulsion	1/206	0.5%
Other unsatisfactory micro-insert location	1/206	0.5%
Initial tubal patency	7/200	3.5%*

*Tubal patency was demonstrated in seven women at the 3-month HSG, but all seven women were shown to have tubal occlusion at a repeat HSG performed 6 months after **Essure** placement.

Table 2
Pivotal Trial
Adverse events that prevented reliance on Essure for contraception

Event	Number	Percent
Expulsion	14/476	2.9%*
Perforation	5/476	1.1%
Other unsatisfactory micro-insert location	3/476	0.6%
Initial tubal patency	16/456	3.5%**

*Fourteen women experienced an expulsion, however nine of these 14 women chose to undergo a second micro-insert placement procedure, which was successful in all nine cases.
** Tubal patency was demonstrated in sixteen women at the 3-month HSG, but all sixteen women were shown to have tubal occlusion at a repeat HSG performed 6-7 months after **Essure** placement

[1] In the Pivotal trial, 657 women initially enrolled in the study. Ninety-nine women subsequently changed their mind about participating. Twenty-three women were subsequently terminated because they did not meet the inclusion criteria, and 17 failed the screening tests. Therefore, 518 underwent the Essure placement procedure. There were a total of 13 women who were lost-to-follow-up in the Pivotal trial.

Appendix A (continued)

Other adverse events or side effects reported as a result of the hysteroscopic placement procedure are shown below in **Tables 3 and 4** for the Phase II and Pivotal studies, respectively.

Table 3
Phase II Study
Adverse events reported on day of placement procedure
(N=233 procedures)

Event	Number	Percent
Band Detachment	3	1.3%
Vaso-vagal response	2	0.9%
Pain	2	0.9%

Table 4
Pivotal Trial
Adverse events and side effects reported on day of placement procedure
(N=544 procedures)

Event	Number	Percent
Cramping	161	29.6%
Pain	70	12.9%
Nausea/vomiting	59	10.8%
Dizziness/light headed	48	8.8%
Bleeding/spotting	37	6.8%
Vaso-vagal response/fainting	7	1.3%
Hypervolemia	2	0.4%
Band Detachment	2	0.4%
Other*	16	2.9%

*Includes: ache (3), hot/hot flashes (2), shakiness (2), uncomfortable (1), weak (1), profuse perspiration (1), bowel pain (1), sleepy (1), skin itching (1), loss of appetite (1), bloating (1), allergic reaction to saline used for distension (1).

In addition, the majority of women experienced mild to moderate pain during and immediately following the procedure, and the majority of women experienced spotting for an average of 3 days after the procedure. Pain was managed in every case with oral non-steroidal anti-inflammatory drugs (NSAIDs) or oral narcotic pain reliever.

Table 5 summarizes all adverse events rated by the Investigators to be at least "possibly" related to the **Essure** micro-insert or micro-insert placement procedure during the first year of reliance on **Essure** in the Pivotal trial (approximately 15 months post-device placement). The percentages presented reflect the number of *events* in the numerator and the number of *women in the trial* in the denominator. While a woman reporting numerous episodes of the same event is represented in the numerator as multiple reports of that event, she is only represented in the denominator once. Consequently, in some cases these percentages over-represent the percentage of *women* who have experienced that event.

Appendix A (continued)

Table 5
Pivotal Trial
Adverse Events by Body Systems, First Year of Reliance*
(N=476 patients implanted with at least one device)

Adverse Events by Body System	Number	Percent
Abdominal:		
Abdominal pain/abdominal cramps	18	3.8%
Gas/bloating	6	1.3%
Musculo-skeletal:		
Back pain/low back pain	43	9.0%
Arm/leg pain	4	0.8%
Nervous/Psychiatric:		
Headache	12	2.5%
Premenstrual Syndrome	4	0.8%
Genitourinary:		
Dysmenorrhea/menstrual cramps (severe)	14	2.9%
Pelvic/lower abdominal pain (severe)	12	2.5%
Persistent increase in menstrual flow	9**	1.9%
Vaginal discharge/vaginal infection	7	1.5%
Abnormal bleeding - timing not specified (severe)	9	1.9%
Menorrhagia/prolonged menses (severe)	5	1.1%
Dyspareunia	17	3.6%
Pain/discomfort - uncharacterized:	14	2.9%

* Only events occurring in $\geq$ 0.5% are reported
** Eight women reported persistent *decrease* in menstrual flow

In the Phase II trial, 12/206 (5.8%) women with at least one micro-insert reported episodes of period pain, ovulatory pain, or changes in menstrual function.

Appendix B: Sample Essure Patient Decision Checklist (FDAd n.d.)

Labeling for Permanent Hysteroscopically-Placed Tubal Implants Intended for Sterilization: Guidance for Industry and Food and Drug Administration Staff

Appendix B: Patient Decision Checklist Example

To the patient considering the Essure System for Permanent Birth Control ("Essure"):
The review and completion of this document is a critical step in helping you decide whether or not to have Essure implanted. You should carefully consider the benefits and risks associated with the device before you make that decision. After reviewing the information in this brochure, please read and discuss the items in this checklist with your doctor. You should not initial or sign the document, and should not undergo the procedure, if you do not understand each of the elements listed below.

_____

Birth Control Options

I understand that Essure is a permanent form of birth control (referred to as "sterilization"). I understand that sterilization must be considered permanent and not reversible.

I was told about other permanent sterilization procedures, such as surgical bilateral tubal ligation ("getting tubes tied"), and their benefits and risks.

I am aware that there are highly effective methods of birth control which are not permanent and which may allow me to become pregnant when stopped.

Patient Initials _____

Requirements for Essure Placement and Reliance
I understand that I am not a candidate for Essure if:

- I am uncertain about ending my fertility.
- I have had a tubal ligation procedure ("tubes tied").
- I cannot have two inserts placed due to my anatomy.
- I am pregnant or suspect that I may be pregnant.
- I have delivered or terminated a pregnancy within the last 6 weeks.
- I have had a pelvic infection within six weeks prior to the date of the scheduled implantation.
- I have a known allergy to contrast dye used during x-ray procedures.

Essure works as intended only when the devices are successfully placed in both fallopian tubes. I understand that if this is not possible in my case, I may need to undergo a repeat attempt at Essure placement or consider a different form of birth control.

I understand that the placement procedure is only the first step in relying on Essure for birth control. After placement I must:

- Use an alternative form of birth control until my doctor tells me I can stop (typically for 3 months).

Appendix B (continued)

- Schedule and undergo a confirmation test after three months to determine whether I may rely on Essure. I understand that payment for this test may or may not be covered by my insurance company.

I understand that a satisfactory confirmation test is needed before I can rely on Essure alone. I also understand that after the confirmation test my doctor may inform me that I may not be able to rely on Essure. If this occurs, I will have to use an alternative form of contraception.

I understand that based on clinical studies, approximately 8% of women who undergo attempts at Essure placement are not able to rely on the device for contraception.

Patient Initials _____

Pregnancy Risks

I understand that no form of birth control is 100% effective. Even if my doctor tells me I am able to rely on Essure, there is still a small chance that I may become pregnant. Based on clinical studies, the chance of unintended pregnancy for women who have been told they can rely on Essure is less than 1% at 5 years.

I understand that the risks of Essure on a developing fetus have not been established. If I become pregnant with Essure, there may be an increased risk for the pregnancy to occur outside of the uterus ("ectopic pregnancy"). This may result in serious and even life-threatening complications. I understand that after Essure placement, I should contact my doctor immediately if I think I may be pregnant.

Patient Initials _____

What to Expect During the Procedure and the Days Afterwards

I understand that in clinical studies supporting device approval, the following events were reported to occur during the Essure placement procedure and/or in the hours or days following placement:

- Cramping (Reported in up to 30% of procedures)
- Mild to moderate pain (Up to 9-10%) or moderate pain (Up to 13%)
- Nausea/Vomiting (Up to 11%)
- Dizziness/Lightheadedness (Up to 9%)
- Vaginal bleeding (Up to 7%)

If I experience worsening of any of the events listed above or I continue to have the symptoms 1 week after placement, I understand that I should contact my doctor.

Patient Initials _____

Long-Term Risks

I understand that some women may experience continued pain or develop new pain after Essure placement. I understand that I should contact my doctor if abdominal, pelvic or back pain continues for more than 1 week after placement or if I develop the onset of new pain more than 1 week after placement.

Appendix B (continued)

I understand that the Essure implants contain metals including nickel, titanium, iron, chromium, and tin, as well as a material called polyethylene terephthalate (PET). I understand that some women may develop allergic reactions to the device following implantation and have signs or symptoms such as rash and itching. This may occur even if there is no prior history of sensitivity to those materials. I also understand that there is no reliable test to predict ahead of time who may develop a reaction to the device.

I understand that persistent or new pain, and/or allergic reaction may be a sign of an Essure-related problem which might require further evaluation and treatment, including possibly the need to have the devices removed by surgery.

I recognize that other symptoms have been reported to FDA by women implanted with Essure, although they were not seen in the clinical trials supporting Essure approval. The more common symptoms reported include headache, fatigue, weight changes, hair loss and mood changes such as depression. It is unknown if these symptoms are related to Essure or not.

I understand that because Essure contains metals, I should tell all my doctors that I have the device before getting an MRI.

I understand that there is a small possibility that the device could poke through the wall of the uterus or fallopian tubes ("perforation"), and/or move to other locations in the abdomen or pelvis ("migration"). The rate of perforation in studies has ranged from 1% to 4%. The rate for device migration into the abdomen or pelvis has not been determined but its occurrence is uncommon.

I understand that should one of these events occur, the device may become ineffective in preventing pregnancy and may lead to serious adverse events such as bleeding or bowel damage, which may require surgery to address.

I understand that should my doctor and I decide that Essure should be removed after placement, a surgical procedure will be required. In complicated cases, my doctor may recommend a hysterectomy (removal of the entire uterus). I also understand that device removal may not be covered by my insurance company.

Patient Initials _____