

1 **Labeling for Permanent**
2 **Hysteroscopically-Placed Tubal**
3 **Implants Intended for Sterilization**

6 **Draft Guidance for Industry and Food**
7 **and Drug Administration Staff**

8
9 ***DRAFT GUIDANCE***

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13 **Document posted on: February 29, 2016**

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16 publication in the *Federal Register* of the notice announcing the availability of the draft guidance.
17 Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the
18 Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane,
19 rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the
20 notice of availability that publishes in the *Federal Register*.

21
22 For questions about this document, contact the Division of Reproductive, Gastro-Renal, and
23 Urological Devices at 301-796-7030.



U.S. Department of Health and Human Services
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Preface

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DRAFT

Labeling for Permanent Hysteroscopically-Placed Tubal Implants Intended for Sterilization

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance identifies content and format for labeling materials for permanent, hysteroscopically-placed tubal implant devices intended for female sterilization. FDA believes this guidance, when finalized, will help to ensure that a woman receives and understands information regarding the benefits and risks of this type of device.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

Female sterilization is an elective procedure that permanently prevents a woman from becoming pregnant by disrupting the fallopian tubes and preventing fertilization of an egg following ovulation. As sterilization is intended to be an irreversible procedure, it is only appropriate for women who are certain that they wish to permanently end their ability to conceive naturally. Female sterilization is one of the most common procedures in the United States, with more than

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75 500,000 performed per year.¹ The procedure may be performed immediately following delivery
76 of an infant (post-partum sterilization) or at a time not associated with a recent pregnancy
77 (interval sterilization). For decades, female sterilization has been performed by surgical
78 bilateral tubal ligation (BTL) through a laparotomy, a mini-laparotomy, transvaginal approach
79 or at the time of a cesarean delivery, and, more recently, via laparoscopy. During surgical BTL,
80 the fallopian tubes are cut, or various procedures or medical instruments, such as electrosurgical
81 coagulation, implantable clips or rings, are used to physically block or close the fallopian tubes.
82 Surgical BTL is effective immediately, generally safe, requires little to no patient compliance,
83 and is a highly effective method of permanent sterilization. However, there are certain risks of
84 surgical BTL, including, but not limited to, the risks related to general anesthesia, possible
85 physical injury to local organs (e.g., bowel), and bleeding. Some of these adverse events,
86 although uncommon, may result in hospitalization and/or re-operation.²

87
88 In addition to surgical BTL, medical devices have been developed to provide alternative, less-
89 invasive methods of female sterilization through the insertion of permanent implants into a
90 woman's fallopian tubes via a hysteroscopic, non-incisional route. The inserted permanent
91 implants are intended to provide sterilization via physical occlusion and/or the elicitation of a
92 local inflammatory/fibrotic response. This type of device may require a "waiting period" in
93 order to accomplish full occlusion. As the number of hysteroscopic sterilizations with such
94 devices has increased, additional information, including reports of adverse events, has
95 accumulated. This information has included reports of hypersensitivity reactions to the implant
96 materials, persistent pain, irregular vaginal bleeding, fallopian tube or uterine perforation, and
97 intra-peritoneal device migration as well as unintended pregnancy. Some instances of adverse
98 events have resulted in surgical intervention, including device removal.

99
100 On September 24, 2015, FDA convened its Obstetrics and Gynecology Devices Panel of the
101 Medical Devices Advisory Committee to discuss available data regarding benefits, the
102 aforementioned risks, and potential mitigation strategies to prevent or reduce the
103 frequency/severity of the adverse outcomes reported in association with one such device, the
104 Essure System for Permanent Birth Control.³ The Essure System is the only permanent
105 hysteroscopically-placed tubal implant intended for sterilization that is currently marketed in the
106 United States.

107
108 Based on the 2015 Panel meeting, including comments made during the Open Public Hearing
109 portion of the meeting and comments submitted in the associated public docket,⁴ FDA believes
110 that some women are not receiving or understanding information regarding the risks and benefits
111 of permanent, hysteroscopically-placed tubal implants that are intended for sterilization. This
112 draft guidance addresses these concerns. In addition, the Agency will continue to monitor

¹ Chan LM, Westhoff CL. Tubal sterilization trends in the United States. *Fertility and Sterility*, 2010; 94(1): 1-6.

² Jamieson DJ, Hillis SD, Duerr A et al.(2000) Complications of interval laparoscopic tubal sterilization: Findings from the United States Collaborative Review of Sterilization. *Obstet & Gynecol* 96(6): 997-1002.

³ For more information and meeting materials, see

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/ObstetricsandGynecologyDevices/ucm463457.htm>.

⁴ <http://www.regulations.gov/#!docketDetail;D=FDA-2014-N-0736>.

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113 information about potential safety risks and take other steps to ensure they are being adequately
114 conveyed to and understood by physicians and patients.

115
116 FDA is issuing this draft guidance to enable the public to comment on the proposed language for
117 a boxed warning and patient decision checklist that FDA intends to require as part of the product
118 labeling as described below. FDA believes this information will help to ensure that a woman
119 receives and understands the benefits and risks associated with her contraceptive options so that
120 she can make an informed decision as to whether having a permanent implant placed in her
121 fallopian tubes via a hysteroscopic, non-incisional route is the right choice for her.

122 **III. Scope**

123
124 This draft guidance is about the content and format of labeling for permanent, hysteroscopically-
125 placed tubal implants that are intended for sterilization. The guidance applies to all devices of
126 this type, regardless of the insert material composition, location of intended implantation, or
127 exact method of delivery. It is being issued in response to information provided to FDA,
128 including at the 2015 Panel meeting and in the associated public docket, that some women are not
129 receiving or understanding information regarding the risks and benefits of this type of device,
130 including those associated with device implantation and removal. Medical devices used during
131 surgical BTL procedures (e.g., cautery devices, rings, clips) are outside the scope of this
132 guidance.

133
134 The guidance is not intended to include a complete listing of all labeling components for
135 permanent, hysteroscopically-placed tubal implants intended for sterilization. Rather, this
136 guidance specifically focuses on inclusion of a boxed warning and patient decision checklist in
137 the product labeling. Accurate product labeling and effective messaging of that labeling is
138 important to make device users and patients aware of the risks associated with permanent,
139 hysteroscopically-placed tubal implants intended for sterilization. FDA believes that a boxed
140 warning and a patient decision checklist as described in this guidance should be included in
141 labeling under sections 502(a), 201(n), and 502(f)(2) of the Federal Food, Drug, and Cosmetic
142 Act (FD&C Act). FDA intends to require such labeling information as part of a premarket
143 approval (PMA), and intends to work with manufacturers, including of already marketed
144 products, through the PMA and PMA supplement process. We have determined that a boxed
145 warning and a patient decision checklist are particularly effective means of communicating this
146 information to patients. This guidance should be used as a complement to [FDA's "Guidance on
147 Medical Device Patient Labeling"](#) (which describes FDA's current thinking on making medical
148 device patient labeling understandable to and usable by patients), existing regulations, and other
149 relevant guidance documents containing additional labeling recommendations.⁵ FDA requests
150 comment on the wording and content of the recommended boxed warning and patient decision
151 checklist.

⁵ We note that a device is misbranded if its labeling is false or misleading in any particular (section 502(a) of the FD&C Act) or, if applicable, its labeling does not provide adequate warnings (section 502(f)(2) of the FD&C Act). Under section 301(a) of the FD&C Act, it is a prohibited act to introduce or deliver for introduction into interstate commerce any device that is misbranded.

152 **IV. Labeling Components**

153
154 This section contains the wording and content FDA believes should be included in a boxed
155 warning and patient decision checklist in the product labeling of permanent, hysteroscopically-
156 placed tubal implants intended for sterilization. The specific examples referenced in the
157 appendices are written to address the currently marketed device of this type.
158

159 **A. Boxed Warning**

160
161 FDA believes that a boxed warning should be part of physician and patient labeling materials
162 for a permanent, hysteroscopically-placed tubal implant for sterilization and should:
163

- 164
- 165 • Note the types of significant and/or common adverse events that may be associated with
166 the device and its insertion and/or removal procedures, including those noted in clinical
167 trials, as well as those reported in device use experience.
 - 168 • Include a statement noting that these risks should be conveyed to the patient during the
169 woman’s decision-making process.

170 An example of a boxed warning that follows this guidance is provided in **Appendix A**.
171

172 **B. Patient Decision Checklist**

173
174 In addition to the boxed warning, FDA also believes that a patient decision checklist
175 highlighting key risk and benefit information should be included at the end of the patient
176 labeling brochure. The checklist is intended to be reviewed and signed by the patient and
177 physician, and should be printed in a fashion where it can be easily separated from the
178 remainder of the patient information brochure, and upon which pen markings can be
179 permanently made.
180

181 The introduction for the checklist should include a description of the purpose and importance
182 of the checklist, as well as instructions to the patient on how to review and complete the
183 document prior to her decision whether to undergo the permanent implant procedure.
184

185 The body of the checklist should include key items related to the device, its use, and its safety
186 and effectiveness. Items that should be addressed include the following:
187

- 188 • notification of the permanent (and if applicable, irreversible) nature of sterilization in
189 general, and the implant more specifically;
- 190 • recognition of available alternative contraceptive modalities and their safety and
191 effectiveness;
- 192 • situations in which the device should not be used or implanted (e.g., contraindications);
- 193 • steps, if any, that will need to be followed before the implant can be relied upon for
194 contraception, and the importance of compliance with those steps;

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- 195 • information on effectiveness and chances for unintended pregnancy and ectopic
196 pregnancy, including a statement that no contraceptive device is 100% effective;
- 197 • significant and/or common adverse events, including patient-reported outcomes, which
198 may occur during or immediately following device placement;
- 199 • clinically significant longer-term adverse events or outcomes that have been reported in
200 clinical trials or via other device use experience – including significant events that may
201 persist from the time of implantation and those that may appear for the first time later
202 after implantation;
- 203 • a brief discussion of the types of signs, symptoms or events that may represent device-
204 related complications for which the patient should seek prompt evaluation;
- 205 • a disclosure of the device materials and any risks that may be associated with them,
206 including allergy/hypersensitivity and Magnetic Resonance Imaging (MRI) safety
207 information, if applicable; and
- 208 • information related to device removal and/or reversal (e.g., reasons for removal,
209 techniques, outcomes).

210
211 Where applicable, and if known (e.g., based on clinical trial results), probabilities or rates of
212 events should be included within the individual checklist items. The source of the
213 probabilities or rates of events should be identified.

214
215 Each separate item in the body of the checklist should be accompanied by a line for the patient
216 to initial her acknowledgment and understanding of that individual piece of information.

217
218 At the end, the checklist should include a section that summarizes the importance of the
219 information and confirms that the patient has read and understood the material and has had the
220 opportunity to satisfactorily discuss and ask questions of her physician. This should be
221 followed by signature lines for both the patient and physician.

222
223 The FDA recommends that the original signed copy be retained by the physician in the patient
224 records, and that a copy be provided to the patient. The FDA also encourages device
225 manufacturers to develop a plan to audit (and if appropriate, institute steps to improve) the
226 distribution and signing of the checklists as a component of the patient decision-making
227 process, and to periodically update the checklist as additional data is collected with post-
228 market experience.

229
230 **Appendix B** provides an example of a Patient Decision Checklist that follows this guidance.
231

Appendix A: Boxed Warning Example

WARNING: Some patients implanted with the Essure System for Permanent Birth Control have reported adverse events, including perforation of the uterus and/or fallopian tubes, intra-abdominal or pelvic device migration, persistent pain, and allergy or hypersensitivity reactions. Some of these reported events resulted in device removal that required abdominal surgery. This information should be shared with patients considering sterilization with the Essure device during discussion of the benefits and risks of the device.

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280 **Appendix B: Patient Decision Checklist Example**

281

282 To the patient considering implantation of the Essure System for Permanent Birth Control:

283 The review and completion of this form is a critical step in helping you decide whether to have
284 the Essure System procedure and implants. You should carefully consider the benefits and risks
285 associated with the device before you make that decision. This form lists important risks,
286 including those known or reported to be associated with the use of the device based on
287 information from clinical trials, scientific literature, and reports from women who have
288 undergone device placement.

289

290 After reviewing the Essure Patient Information Brochure, please read and discuss this document
291 carefully in consultation with your physician. You should place your initials in the location
292 provided next to each item to indicate that you have read and understood that item. Your full
293 signature at the end of this document means that you have read the materials, that your physician
294 has answered all questions to your satisfaction, and that you understand all statements listed
295 below. You should not sign the form, and should not undergo the procedure, if you do not
296 understand each of the elements listed below.

297

298

299 I understand that the Essure System is a permanent form of birth control (referred to
300 as “sterilization”) and that by electing to have the Essure device implanted in my fallopian
301 tubes, I am deciding to permanently end my ability to become pregnant. I understand that
302 sterilization must be considered permanent and not reversible.

303

Patient Initials _____

304

305 I am aware that there are temporary, highly effective methods of birth control
306 that are available, which may allow me to bear a child in the future.

307

308

Patient Initials _____

309

310 I was told about other alternative permanent sterilization procedures, such
311 as bilateral tubal ligation (“getting tubes tied”), and their benefits and risks.

312

313

Patient Initials _____

314

315 I understand that I am not a candidate for the Essure System if:

316

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

325

Patient Initials _____

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326 I understand that successful placement of the Essure devices into both fallopian
327 tubes may not be possible in some women. If that is the case with me, I may need
328 to undergo a repeat attempt at Essure device placement or consider a different form of
329 birth control, because the system works only when both Essure devices are successfully
330 implanted.

331 Patient Initials _____

332
333 I understand that having the insert procedure is only the first step in the process
334 of the Essure System and that I must:

- 335 • Use an alternative form of contraception (e.g., intrauterine device (IUD),
336 birth control pill or implant) until my physician tells me I can
337 stop (typically for 3 months, but possibly longer).
- 338 • Schedule and undergo the confirmation test recommended by my physician
339 after three months to ensure that my inserted Essure devices are in the proper
340 location and that the fallopian tubes are blocked. I understand that this is a
341 critical part of the Essure System procedure and sterilization process, and that
342 payment for this test may or may not be covered by my insurance company.

343
344 Patient Initials _____

345
346 I understand that even after the confirmation test, my physician may inform
347 me that I may not be able to rely on the Essure System for permanent contraception.
348 If this occurs, I will have to use an alternative form of contraception. In a recent
349 study with the Essure device, over 90% of women who underwent attempts at
350 device placement were able to rely on the device for contraception.

351
352 Patient Initials _____

353
354 I understand that no form of birth control is 100% effective and that even if my
355 physician tells me I am able to rely on the Essure System, there is still the small
356 possibility that I may become pregnant. Based on currently available data, the
357 chance of unintended pregnancy for women whose confirmation tests indicate
358 that the devices have been successfully placed and the fallopian tubes have
359 been blocked is less than 1%.

360
361 Patient Initials _____

362
363 I understand that the risks of the Essure device on a developing fetus during
364 pregnancy have not been established. I also understand that I may be at increased
365 risk for a pregnancy occurring outside of the uterus (“ectopic pregnancy”),
366 which may result in serious and even life-threatening complications. I understand
367 that I should contact my physician immediately if there are any indications
368 I may be pregnant.

369 Patient Initials _____

370
371

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372 I understand the following events were reported to occur during the Essure procedure and/or in
373 the hours or days following insertion. The rates included below in parentheses were reported
374 during the original Essure System studies:

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

380

381 If I experience any of these events listed above, and they persist or worsen in
382 the days to weeks following implantation, I understand that I should promptly
383 consult my physician as they may be a sign of an Essure-related problem
384 that needs prompt attention.

385

Patient Initials _____

386

387 I understand that following Essure System placement, some women may experience
388 adverse events including persistent pain, device puncture of the uterus and/or
389 fallopian tubes (“perforation”), or movement of the device into the abdomen or
390 pelvis (“intra-peritoneal migration”). There have also been reports of allergy or
391 hypersensitivity reactions in some women.

392

393 I understand that if I experience any of the following, I should contact my physician:

- 394 • Abdominal, pelvic or back pain that develops or persists more than 1
395 week following insertion. Data suggest that for those women who do
396 experience pain during and/or immediately after the procedure, most will have
397 their symptoms resolve within a few days, and 99% will have their symptoms
398 resolve within 1 week.
- 399 • Signs or symptoms consistent with an allergic or hypersensitivity
400 reaction. These may include persistent changes in my skin (rash, itching)
401 but may also include other persistent symptoms such as chest pain,
402 palpitations, breathing difficulties or wheezing, and intestinal discomfort
403 such as nausea, diarrhea, and vomiting. These types of events, although
404 not reported in the clinical trials supporting device approval, have been
405 reported by women implanted with the Essure System.
- 406 • Other signs or symptoms that continue or recur including joint or
407 muscle pain, muscle weakness, excessive fatigue, hair loss, weight
408 changes, and mood changes. These types of events, although not reported
409 in the clinical trials supporting device approval, have been reported to FDA by
410 women implanted with the Essure System.

411

412 I understand that these may be signs of an Essure-related problem, which may
413 require prompt evaluation and intervention, including possibly the need for Essure
414 device removal by surgery.

415

Patient Initials _____

416

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418 The Essure System contains metals including nickel, titanium, iron, chromium,
419 and tin, as well as a material called polyethylene terephthalate (PET). I understand
420 that some women may develop allergic or hypersensitivity reactions to the device
421 following implantation, even if they have no prior history of sensitivity to those
422 materials. I also understand that there is no reliable test to predict ahead of time
423 who may develop a reaction to the device.

424
425 Patient Initials _____
426

427 I understand that in some patients, the Essure device can move after placement.
428 I understand there is a possibility that the device could poke through the wall
429 of the uterus or fallopian tubes (“perforation”), and/or travel to other locations
430 in the abdomen or pelvis (“migration”). The rate of perforation in the original
431 Essure System study and several subsequent studies was 1% or less. However,
432 some studies have reported rates up to 3-4%. The rate for device migration into
433 the abdomen or pelvis has not been determined. However, reports of such
434 movement have been rare. I understand that should one of these events occur,
435 the device may become ineffective in preventing pregnancy and may lead to
436 serious adverse events such as bleeding or bowel damage, which may require
437 surgery to address.

438 Patient Initials _____
439

440 I understand that should my physician and I decide that the Essure System
441 should be removed after placement, I will require a surgical procedure and in
442 complicated cases, my physician may recommend a hysterectomy (removal of
443 the entire uterus). I also understand that device removal may not be covered
444 by my insurance company.

445 Patient Initials _____
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CONFIRMATION OF DISCUSSION OF RISKS

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Patient: With my signature below, I acknowledge that I have received and read the Essure System for Permanent Birth Control Patient Information Brochure, and that I have had ample time to discuss the items contained within it and on this form with my physician. I have had the opportunity to ask questions and understand the benefits and risks of the device and procedure, and understand that alternative methods of contraception are available. I voluntarily choose to proceed with placement of the Essure device.

Patient Signature and Date

Physician: With my signature below, I acknowledge that I have discussed the benefits and risks of the Essure device and procedure as described in the Essure System for Permanent Birth Control Patient Information Brochure as well as this document. I have also explained the benefits and risks of other contraceptive methods. Should device removal become necessary, I may perform the removal myself, or provide a referral to a physician who is willing and able to perform device removals. I have encouraged the patient to ask questions, and I have addressed all questions.

Physician Signature and Date