Guidance for Industry and for FDA Reviewers/Staff

Guidance for the Content of Premarket Notifications for Penile Rigidity Implants

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U.S. Department Of Health And Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Urology and Lithotripsy Devices Branch
Division of Reproductive, Abdominal, Ear, Nose and Throat, and Radiological Devices
Office of Device Evaluation

GRZAN

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Chief, Urology and Lithotripsy Devices Branch, HFZ-470, 9200 Corporate Blvd., Rockville, Maryland 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance, please contact John H. Baxley at (240) 276-4161 or by electronic mail at john.baxley@fda.hhs.gov.

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World Wide Web/CDRH home page: *http://www.fda.gov/cdrh/ode/guidance/177.pdf*, or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 177 when prompted for the document shelf number.

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1. Introduction

A. Background

The purpose of this guidance document is to identify information that should be provided to the Food and Drug Administration (FDA) in a premarket notification (510(k)) to support a determination of substantial equivalence for a penile rigidity implant.

B. Device Design/Principle of Operation

A penile rigidity implant consists of a pair of semirigid rods or cylinders that are surgically implanted in the corpora cavernosa of the penis in patients diagnosed as having erectile dysfunction. The purpose of this device is to provide adequate penile rigidity for vaginal intercourse. Several different noninflatable designs are included under this device classification:

- *rod prostheses*, which typically consist of a flexible, solid cylinder of polymer material;
- *malleable prostheses*, which typically consist of a flexible polymer cylinder that incorporates an internal metal core;
- *single hinged prostheses*, in which each rod incorporates a highly flexible segment of material to enable the patient to position the penis downward for concealment under his clothes; and
- *multiple hinged prostheses*, which typically consist of a series of hinged segments, encapsulated in a polymer sheath.

C. Regulatory History

Penile rigidity implants are preamendments devices which were originally classified into class III. Based on new information known regarding these devices, FDA published a proposed rule on December 16, 1997 proposing reclassification of the penile rigidity implant to class II (62 FR 65770). On February 2, 2000, FDA published a final rule in the Federal Register reclassifying penile rigidity implants into class II (65 FR 4881).

D. Devices Not Included

This guidance document does not address penile inflatable implants, which are class III devices for which a proposed rule to require the submission of premarket approval (PMA) applications was published on April 28, 1993.

E. Additional Sources of Information

General guidance concerning the information required to be in a 510(k) may be obtained from the Center for Devices and Radiological Health's Division of Small Manufacturers Assistance (DSMA) at (800) 638-2041 or (301) 443-6597, or at it Internet address (*http://www.fda.gov/cdrh/dsma/dsmamain.html#contents*).

For further information, please contact DSMA or:

Urology and Lithotripsy Devices Branch (ULDB)
Division of Reproductive, Abdominal, Ear, Nose
and Throat, and Radiological Devices
Center for Devices and Radiological Health
9200 Corporate Boulevard (HFZ-470)
Rockville, Maryland 20850
(301) 594-2194 (phone)
(301) 594-2339 (fax)

2. Sponsor/Device Identification

FDA regulations (21 CFR 807.87) prescribe information that must appear in each 510(k) submission. This information includes:

A. Sponsor/Manufacturer Information

The name, contact person, address, telephone number, and (if available) facsimile number of both the sponsor of the 510(k) application and (if different from the sponsor) the device manufacturer.

B. Proposed Device

The trade or proprietary name of the device proposed for marketing, as well as the common device name, i.e., penile rigidity implant.

C. Predicate Device

The legally marketed device(s) to which the new device is being compared. To be as specific as possible, the 510(k) should include the following information to identify each predicate device and support the claim substantial equivalence:

- Trade/proprietary name,
- Model number,
- Manufacturer,
- 510(k) reference number (if known) or preamendments status,

- Intended use,
- Technological characteristics/performance specifications, and
- Labeling.

3. Classification/Product Code

The Code of Federal Regulations (CFR) number, class, and product code applicable to the penile rigidity implant (listed below) should be provided in the 510(k):

- CFR Number: 21 CFR 876.3630
- Regulatory Class: Class II (special controls)
- Product Codes: 78 FAE (penile prosthesis) *or* 78 FTQ (rigid rod penis prosthesis)

Product code 78 FAE refers to the malleable and hinged prostheses, whereas 78 FTQ refers to simple, solid cylinders.

4. Special Controls

As stated in the final rule reclassifying the penile rigidity implant into class II, this guidance document† is the special control for this device.

† *This guidance document describes a means by which penile rigidity implants may comply with the requirement of special controls for class II devices. Designation of this guidance document as a special control means that manufacturers attempting to establish that their device is substantially equivalent to a predicate device should demonstrate that the proposed device complies with either the specific recommendations of this guidance or some alternative control that provides equivalent assurances of safety and effectiveness.*

5. Device Description

A. Reason for 510(k)

The sponsor should clearly state the reason for the submission of the 510(k), e.g., new device model, change in intended use, or design modifications to an existing penile rigidity implant.

B. Intended Use

The 510(k) should provide a clear statement of the proposed device's intended use, such as:

"The [*device trade name*] is intended for implantation into the corpora cavernosa of the penis in men who are diagnosed as having erectile dysfunction. The prosthesis is implanted to provide adequate penile rigidity for sexual intercourse."

The intended use should be identically worded in the following sections of the 510(k):

- the physician's labeling,
- the "Indications for Use" form, and
- (if provided) the "510(k) Summary."

C. Technical Characteristics

The sponsor should provide a technical summary of the device (or device modification, if applicable). This section of the 510(k) should include, but not be necessarily limited to, the following information:

- General description of the entire device, detailing its principle of operation.
- Listing of all available sizes.
- Description of the device's constituent components/subassemblies.
- Listing of all device materials, identifying those that are patient-contacting.
- List of all accessories.
- Diagrams of the device and accessories, with all key dimensions and component materials well-marked and sufficient cross section or magnified diagrams to show adequate detail.
- Description of the device's implantation instructions.
- Description of the device's activation/deactivation instructions (i.e., patient's instruction for device operation).

D. Sterilization

The following information regarding the device's sterilization process should be provided: (i) the method of sterilization; (ii) the protocol used to validate the sterilization cycle; (iii) a description of the packaging materials; (iv) the residual levels of ethylene oxide (≤ 25 ppm), ethylene chlorohydrin (≤ 25 ppm), and ethylene glycol (≤ 500 ppm) remaining on the device after the sterilization quarantine period (if ethylene oxide sterilization is used); and (v) the radiation dose (if gamma radiation sterilization is used). Additionally, the method used to routinely evaluate this device for pyrogenicity (e.g., LAL or rabbit test) should be stated.

6. Claim of Substantial Equivalence

In order to permit a determination of substantial equivalence, all intended uses and technological characteristics, including performance test results and labeling, should be compared to a legally marketed device. It is recommended that such comparisons be presented in tabular format.

7. Performance Testing

A. General Considerations

During its functional lifetime, a penile rigidity implant will be subjected to a variety of stresses. These stresses occur during typical daily activities, during the act of intercourse, and at rest. To determine if a proposed device design can withstand these stresses, performance testing should be performed. This testing (i) should be conducted using an appropriate number of final, sterilized samples, (ii) should separately evaluate the performance of the largest and smallest device sizes being proposed, and (iii) should be compared to those of a legally marketed predicate device whenever possible.

Based on the general design requirements of a penile rigidity implant, FDA believes that the following tests should be considered. However, 510(k) sponsors should be aware that modifications or additions to this test plan may be needed for unique device designs.

B. Simulated Life/Fatigue Testing

The purpose of Simulated Life/Fatigue Testing is to determine whether the proposed device can withstand the cyclical forces that occur when a patient alters the position of his penis over the expected lifetime of the device. The following information should be considered when designing this test:

- Test design should simulate, as closely as possible, the actual environment and stresses experienced by the device post-implantation. The maximum test stresses should be at least equal to the anticipated use stresses, and should be applied to those sections of the device that will experience the highest stresses in use.
- The devices should be cycled until either failure occurs or a predetermined cycle limit is reached. Any predetermined limit should be justified to be at least equal to the anticipated number of cycles of the device's expected service life.
- The length of the device should be measured periodically during this testing, with any changes reported.
- The maximum bend angle should be measured periodically during this testing, with any changes reported.
- The outer covering of the device should be examined periodically during this testing for any evidence of wear, voids, tears, crazing, or other evidence of physical damage.

C. Positioning/Concealability Testing

The purpose of Positioning/Concealability Testing is to determine the ease and consistency with which the proposed device can be bent and positioned over its expected lifetime. The following information should be considered when designing this test:

- Both the force required to bend the device and the ability of the device to be positioned and remain at particular angles (representative of actual "rigid" and "flaccid" states) should be measured.

- These measurements should be taken at periodic intervals during the Simulated Life/Fatigue Testing.

D. Buckling Testing

The purpose of Buckling Testing is to determine if the device has sufficient column strength to allow the device to be used as intended (i.e., for vaginal penetration/intercourse). The test should quantitatively measure the buckling strength of the device at periodic intervals during the Simulated Life/Fatigue Testing, and be compared to a justified, predetermined, performance requirement.

E. Tip Extender Joint Strength Testing

Tip Extender Joint Strength Testing is only applicable to devices that have optional tip extenders. The purpose of this testing is to verify that the connection between the tip extender(s) and the main body of the device will remain intact during the expected life of the device.

F. Biocompatibility Testing

The 510(k) should contain either results of biocompatibility testing performed on all patient-contacting materials, or a certification stating that each material formulation used in the proposed device is identical to that used in another, identified, legally marketed device with a similar degree of patient contact. Penile rigidity implants are considered to be permanent, tissue/bone contacting, implanted devices, and testing should include, but is not limited to, cytotoxicity, sensitization, irritation (or intracutaneous reactivity), acute systemic toxicity, genotoxicity, and implantation testing (≥ 90 days). If the general formulation of the patient-contacting material has no prior history of use as a long-term implant, the sponsor should also evaluate the material for chronic toxicity and carcinogenicity.

For additional information on the above recommendations for biocompatibility testing, please refer to the document entitled "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part-1: Evaluation and Testing'" (5/1/95). A copy of this guidance document may be obtained from DSMA.

G. Clinical Testing

Clinical testing is only recommended for penile rigidity implants that are significantly different in design, materials, control method, operating principle, or intended use as compared to devices already on the market. In such circumstances, the results of clinical testing of the device should be submitted to evaluate whether the proposed implant is as safe and as effective as predicate penile rigidity implants.

FDA recommends that the following information should be considered when designing a clinical study for a penile rigidity implant:

- The objectives of this clinical study should be (i) to evaluate the potential of the device to fail or cause other complications that necessitate either surgical removal or medical intervention (e.g., infection, erosion, migration, extrusion, mechanical malfunction, patient dissatisfaction, prolonged or intractable pain, urinary obstruction, etc.); and (ii) to assess the ability of the device to provide adequate penile rigidity for sexual intercourse.

- The study should enroll a minimum of 50 patients using appropriate inclusion/exclusion criteria, and evaluate the effects of repeated device use post-implantation. Each patient should be adequately screened using standard methods as having erectile dysfunction prior to receiving the implant. Furthermore, each subject should complete an appropriate sexual function questionnaire, for later comparison to the post-treatment results for evaluation of device performance. Prior to device implantation, the subject should be provided with detailed patient labeling, as described in Section 8.B. of this document.

- The investigators should record appropriate data during the implantation procedure, such as: insertion site, accessories and tools used (if any are sold with the device), implant size used, and assessment of device function/anatomical outcome.

- Follow-up examinations should be scheduled to allow the investigating physician to physically assess for the incidence of any complications, as well as the anatomical placement of the prosthesis. Additionally, if the patient has begun to use his prosthesis for sexual intercourse, he should fill out the post-treatment sexual function questionnaire at the exam. These follow-up exams should occur at the following time frames: (i) at the time that the patient is instructed to begin sexual intercourse (e.g., 6 weeks post-surgery); and (ii) 6 months post-surgery. Furthermore, the protocol should inform study subjects to immediately notify the investigator if any problems are encountered with the use of the device, and to receive additional follow-up exams if deemed necessary. Lastly, at the end of the follow-up period, each patient should be questioned regarding his level of satisfaction with the various qualities of the device (i.e., concealability, rigidity, length, girth, flaccidity, etc.). Detailed case report forms should be developed to encourage the collection of all data specified in the protocol.

- Outcomes should be analyzed according to the following variables: etiology of erectile dysfunction, whether or not this is the patient's first penile implant, frequency of device usage post-implantation, investigational site, implant size, and incision site.

Any U.S. clinical investigation of a penile rigidity implant that is not legally marketed must be conducted in accordance with the investigational device exemptions (IDE) regulations for a significant risk device. Reports of foreign clinical experience are acceptable provided that the investigation was conducted in accordance with the provisions of the IDE regulations regarding the protection of human research subjects (commonly referred to as the "Declarations of Helsinki"), and the data are applicable to the U.S. population and medical practice. When planning a clinical trial, consult the Urology and Lithotripsy Devices Branch

prior for guidance on the appropriate study design to address the particular technological characteristics offered by the proposed penile rigidity implant.

8. Labeling

A. General Labeling Considerations

Proposed labels, labeling, and any promotional information sufficient to describe the proposed penile rigidity implant, its intended use, and its directions for use should be submitted in the 510(k), consistent with 21 CFR 807.87(e). The label of the device packaging must bear the prescription device statement in accordance with 21 CFR 801.109(b)(1) under the authority of section 520(e) of the Federal Food, Drug and Cosmetic Act:

> "CAUTION: Federal law restricts this device to sale by or on the order of a physician."

Listed below are available sources that may provide useful information regarding the information to be included in the labeling of medical devices: (1) "Device Labeling Guidance," ODE Blue Book Memorandum #G91-1; (2) "Labeling: Regulatory Requirements for Medical Devices," HHS Publication FDA 89-4203; and (3) "Write It Right: Recommendations for Developing User Instruction Manuals for Medical Devices Used in Home Health Care," HHS Publication FDA 93-4258. This information is available from DSMA.

B. Physician Labeling

The following information should be included in the physician labeling for penile rigidity implants:

Device labeling for the penile rigidity implant should include the device name; manufacturer's name, address, and telephone number; the prescription device statement; intended use; and a description of the device (including dimensional specifications). Penile rigidity implants should be labeled as sterile, non-pyrogenic, single use implants. Physicians should be instructed not to resterilize the device.

The intended use statement should include the specific indications for use and identification of the target populations for whom this device is appropriate.

The labeling should include warnings describing the known and potential risks of penile rigidity implants, such as infection, erosion, migration, extrusion, mechanical malfunction, patient dissatisfaction, adverse tissue reaction, prolonged or intractable pain, urinary obstruction, silicone particle migration, and other complications (e.g., post-operative bleeding, hematoma, penile edema, penile necrosis/gangrene, perforation of the corpora or

the urethra, inability to adequately dilate the corpora, incorrect sizing of the implant, and tearing or ripping of the device during implantation).

The warnings section of the physician labeling should include a list of existing medical conditions which may increase the risk of infection (i.e., diabetes, spinal cord injuries, open sores or skin infections in the region of the surgery, or urinary tract infection).

The physician labeling should warn that infection that fails to respond to antibiotic therapy may result in removal of the implant, that implantation of a new device may be contraindicated at that time, and that infection followed by explantation of the device may result in scarring which may make subsequent reimplantation more difficult.

The labeling should describe the types of mechanical malfunctions that could occur with the device.

The labeling should recommend that physicians counsel patients on the expected post-operative course of pain, including severity and duration, to give patients a sense of the normal healing process.

The labeling should state that since penile rigidity implants are subject to wear, eventual failure is expected over time and they should not be considered lifetime implants. Where possible, the labeling should state the anticipated surgical revision rate of the implant.

The directions for use should contain comprehensive instructions regarding the pre-operative, peri-operative and post-operative procedures to be followed, and include information on how to minimize anticipated complications (i.e., infection, erosion, migration, extrusion, mechanical malfunction, urinary obstruction, silicone particle migration, and other complications). This information includes but is not necessarily limited to:

- a description of any training necessary for the surgical team;
- a description of the appropriate measures to reduce the likelihood of infection, including the use of sterile techniques and antibiotic prophylaxis to prepare the patient, the operating room, and the implant;
- instructions for implantation, including possible surgical approaches, implant sizing, device handling, and intraoperative test procedures to ensure implant functionality and proper placement/fit; and
- instructions for follow-up, including recommendations about patient antibiotic prophylaxis during the post-implant period or during any subsequent dental or other surgical procedures, proper care for the surgical site during the healing period, determining when patients are ready to attempt intercourse, and evaluating proper functionality and anatomical placement/fit.

The physician labeling should instruct the urologist or implanting surgeon to provide the implant candidate with the patient labeling **prior** to surgery, to allow each patient

sufficient time to review the information about the device and the procedure and discuss this information with his physician and sexual partner.

C. Patient Labeling

The following information should be included in the physician labeling for penile rigidity implants:

Patient labeling should be provided which includes the information needed to give prospective patients realistic expectations of the benefits and risks of device implantation. This information should aid potential recipients in making informed decisions prior to implantation, as well as educate patients on how to recognize and minimize the potential risks of penile rigidity implants. Such information should be written and formatted so as to be easily read and understood by most patients (i.e., $\leq 7^{th}$ grade reading level), and should be provided to patients **prior** to scheduling implantation so that each patient has sufficient time to review the information and discuss it with his physician and sexual partner. Technical terms should be kept to a minimum and should be defined if they must be used.

The indications for use and relevant contraindications, warnings, precautions and adverse effects/complications should be described using terminology well known and understood by the average layperson.

The anticipated benefits and risks associated with the device should be provided to give the patient realistic expectations of device performance and potential complications. The known, suspected, and potential risks of device implantation should be identified, and the consequences of these risks and possible methods of resolution should be described. Known and potential complications associated with penile rigidity implants include: infection, erosion, migration, extrusion, mechanical malfunction, patient dissatisfaction, adverse tissue reaction, temporary and chronic pain, urinary obstruction, silicone particle migration, and other complications (e.g., post-operative bleeding, hematoma, penile edema, penile necrosis/gangrene, perforation of the corpora or the urethra, inability to adequately dilate the corpora, incorrect sizing of the implant, and tearing or ripping of the device during implantation).

The patient labeling should inform the patient of the following information regarding the risk of infection:

- As with any surgical implantation, an infection may develop after surgery. The physician will take steps to reduce the likelihood of infection. These steps may include using antibiotics to flush the surgical site during surgery, as well as appropriate antibiotics given before and after the surgery. Men with diabetes, spinal cord injuries, open sores or skin infections in the region of surgery, or urinary tract infections may have an increased risk of an infection associated with the device.
- If the infection cannot be treated by antibiotics, it may be necessary to remove the prosthesis. In this case, it may not be possible to implant a new device. In addition,

infection that causes the device to be removed may also cause scarring which may make implanting a new device difficult or impossible.

Patients should be warned that failure to obtain timely medical evaluation and treatment for erosion, migration, or extrusion may result in substantial worsening of the condition, infection, and/or loss of tissue.

The patient labeling should describe the types of mechanical malfunction that could occur with the device.

The patient labeling should inform the patient of the following information regarding the potential outcome of a penile rigidity implant:

- Implantation of a penile prosthesis may result in penile shortening, curvature, or scarring.
- The prosthetic erection may differ from the patient's original, natural erection in that it may be shorter, less firm, have less girth, or have reduced sensation.
- Realistic cosmetic expectations should include the potential for skin scarring, lack of concealability (due to the constant presence of the rigid/semirigid rods), and lack of rigidity to the glans.
- The implant will not enhance or restore libido, penile sensation, or the ability to have an orgasm and ejaculate.
- The device implantation procedure is likely to damage or destroy any previous erectile capability.

The patient labeling should include a brief description of the available alternative therapies for the patient's condition, including less invasive treatments and the associated benefits and risks of each. The patient should be advised to contact his physician for more information on whether any of these alternatives might be appropriate given the patient's specific condition.

The patient labeling should include instructions on how to care for and use the device. This information should include the expected duration of recovery from surgery, when to resume intercourse following implantation, how to urinate and care for the implant and surgical site during the healing period, warnings against certain actions that could damage the device, the conditions that require physician intervention, who to contact if questions arise, and any other relevant information.

Patients should be informed that penile rigidity implants are subject to wear due to normal daily activities, and that eventual failure is expected over time. Therefore, these implants should not be considered lifetime prostheses. Where possible, the labeling should state the anticipated surgical revision rate of the implant.

D. Promotional Literature

Any promotional literature regarding the proposed device should be submitted in the 510(k) for review.

9. Other Administrative Requirements

Each 510(k) submission should contain the following administrative items:

- a completed "Indications for Use" form;
- a signed "Truthful and Accurate Statement;" and
- either a "510(k) Summary" or "510(k) Statement."

Information regarding each of the above items is available from DSMA.

10. Device Modifications

Guidance concerning the premarket notification requirements for device modifications is available in the document entitled "Deciding When to Submit a 510(k) for Change to an Existing Device" (1/10/97). A copy is available from DSMA or CDRH's Internet address (*http://www.fda.gov/cdrh/ode/510kmod.html*).