Guidance for Industry

Guidance for the Content of Premarket Notifications for Intracorporeal Lithotripters

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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

Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to the 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 contact Donald St.Pierre at 301-594-2194 or by electronic mail at djs@cdrh.fda.gov.

Additional Copies

World Wide Web CDRH specific page:
http://www.fda.gov/cdrh/ode/ehlguide.pdf, or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 2235 when prompted for the document shelf number.

Table of Contents

1. Introduction

A. Background

The purpose of this guidance document is to identify the 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 intracorporeal lithotripters. An *intracorporeal* lithotripter is a device that is used to fragment urinary (i.e., kidney, ureter, and bladder) and biliary tract stones. These devices are placed at the stone location via an endoscope or laparoscope. This device class includes, but is not necessarily limited to, electrohydraulic, pneumatic, and ultrasonic lithotripters. These devices are preAmendment class III devices that the Agency is now proposing to downclassify to class II

B. Devices Not Included

This guidance document does not address extracorporeal lithotripters or mechanical lithotripters. Guidance on the regulatory recommendations of urological extracorporeal shock wave lithotripters (SWLs) is available in the document entitled "Guidance for the Contents of Premarket Notifications (510(k)s) for Extracorporeal Shock Wave Lithotripters Indicated for the Fragmentation of Kidney and Ureteral Calculi." Guidance on the regulatory recommendations of mechanical lithotripters is available in the document entitled "510(k) Checklist for Mechanical Lithotripters and Stone Dislodgers used in Gastroenterology and Urology."

C. 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 its Internet address (*http://www.fda.gov/cdrh/dsma/dsmamain.html#contents*).

For further information, contact DSMA or:

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Division of Reproductive, Abdominal, Ear, Nose
and Throat, and Radiological Devices
Center for Devices and Radiological Health
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(301) 594-2194 (phone)
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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., electrohydraulic, pneumatic, and ultrasonic lithotripters.

C. Predicate Device

The legally marketed device(s) to which the proposed 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 of substantial equivalence:

- Trade/proprietary name,
- Common/usual name (electrohydraulic, pneumatic, or ultrasonic lithotripter),
- Model number,
- Manufacturer,
- 510(k) reference number (if known),
- Intended use,
- Technological characteristics/performance specifications, and
- Labeling.

3. Classification/Product Code

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

- CFR Number: 21 CFR 876.4480
- Regulatory Class: Class II (special controls) *[pending Final Rule for reclassification]*
- Product Code: 78 FFK

(Note: The product code for electrohydraulic lithotripters, FFK, has been expanded to include ultrasonic lithotripters which were previously unclassified. The product code, FEO, previously used for ultrasonic lithotripters, will no longer be utilized)

4. Special Controls *[pending Final Rule for reclassification]*

This guidance document serves as the special control for these devices†.

† *This guidance document describes a means by which intracorporeal lithotripters 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 intracorporeal lithotripter should demonstrate that the proposed device complies with either the specific recommendations of the guidance or some alternate 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 intracorporeal lithotripter, change in intended use, or design modifications to an existing intracorporeal lithotripter.

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 to fragment urinary (i.e., kidney, ureter, and bladder) and biliary tract stones."

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) and its major components. This section of the 510(k) should include, but not necessarily be limited to, the following information:

- General overview of the entire system.
- Diagrams of the system and its major components.
- Description of all safety features.
- Description of each of the system's major components/subassemblies.
- Description of the system's software/firmware (if applicable) in accordance with the FDA guidance document entitled "Guidance for the Content of Premarket

Submissions for Software Contained in Medical Devices" (5/29/98) (available from DSMA or its Internet address).

- Description of the method(s) used to verify electrical safety and electromagnetic compatibility.
- Comparative descriptions of each of the device configurations for which marketing clearance is proposed.

6. Claim of Substantial Equivalence

In order to permit a determination of substantial equivalence, all intended uses, technological characteristics, 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. Conformance to Standards

Conformance to consensus standards is not required for 510(k) clearance, however if the electrical safety testing cited in section 8.D.4 is conducted using an FDA recognized standard, then conformance to the standard can be accomplished by submitting "declarations of conformity" in the 510(k). For guidance on the preparation of declarations of conformity to recognized standards, manufacturers should refer to the following documents (available from DSMA or the listed CDRH Internet addresses):

> "A New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications" (3/20/98). (*http://www.fda.gov/cdrh/reengine.html*)
>
> "Guidance on the Recognition and Use of Consensus Standards" (2/19/98). (*http://www.fda.gov/cdrh/modact/modguid.html*)

8. Performance Testing

Manufacturers of intracorporeal lithotripters should submit the results of the following performance tests to demonstrate substantial equivalence between the proposed and predicate devices:

A. Diagrams, Dimensions, and Materials

Provide diagrams of the device, its components/subassemblies, and any accessories (if applicable), with all key dimensions and component materials well-marked. Multiple diagrams are usually necessary to show adequate detail. If a range of probe sizes is to be marketed, the dimensions of each size should be provided separately. A table listing all materials of the intracorporeal lithotripter should be provided, and those that are patient contacting should be specified.

B. Biocompatibility Testing

The results of biocompatibility testing performed on all body-contacting materials, or a certification stating that each material formulation used is identical to that used in a legally marketed device with a similar degree of patient contact, should be submitted. If used transurethrally, intracorporeal lithotripters are considered to be short-term, mucosal membrane contacting, surface devices. Testing for these devices should include, but is not limited to, cytotoxicity, sensitization, and irritation (or intracutaneous reactivity). If the devices are used percutaneously, they are considered to be short-term, indirect blood path contacting, external communicating devices. Testing for these devices should include, but is not limited to, cytotoxicity, sensitization, irritation (or intracutaneous reactivity), acute systemic toxicity and hemocompatibility.

For additional information on biocompatibility, 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.

C. Mechanical Reliability Performance Characteristics

All intracorporeal lithotripters, regardless of type, should meet specific safety and effectiveness criteria. Recommendations for performance testing to illustrate a device's ability to meet these criteria are given below. Sponsors should be aware that these recommendations are not all-inclusive and, for some device designs, additional testing may be required to demonstrate substantial equivalence to a predicate device. Sponsors should be further aware that, in cases of device designs that are significantly different (e.g., new mechanism of action, etc.) from previously marketed devices, clinical data may be required (see Section 8.D.).

All testing should be on finished, sterilized samples and the test results should be compared to those of a legally marketed predicate device whenever possible. Testing should be performed separately for each probe size, unless adequate justification is provided. The following tests should be considered for an intracorporeal lithotripter:

1. Stone Breakage Testing:

The purpose of this testing is to determine whether the proposed device can adequately break/crush stones. A statistically significant number of urinary tract stones, or a justified model material, should be used in this test. The testing should demonstrate that the device can fracture stones under simulated use conditions. An example of a simulated use condition would be breaking a stone under water/saline through a flexible endoscope that has been passed through a model of the biliary/urinary tract.

2. Tissue Perforation Testing:

The purpose of this testing is to demonstrate that the device does not pose an unreasonable risk of tissue damage. This testing should consist of operating the device with the probe in direct contact with appropriate tissue (e.g., explanted ureter and/or kidney tissue) and evaluating any clinically significant damage. An animal model may also be acceptable for this testing.

3. Probe Life Testing:

The purpose of this testing is to demonstrate the ability of the probes, if they are to be resterilized and reused, to withstand the recommended number of resterilizations and still successfully break stones. These data should also be used to make specific recommendations in the labeling on the expected life of a probe. If the probes are for single use only, this testing may be omitted as long as the stone breakage testing has been successfully performed.

4. Electrical Safety Testing:

Data generated from this testing should address electrical safety concerns (e.g., leakage current, grounding, isolation, etc.) **or** the sponsor should provide a certification that the finished product meets all applicable requirements specified in the latest version of a recognized electrical standard for medical devices (e.g., ANSI/AAMI HF-18, ANSI/AAMI ESI-1985, IEC60601-1-1 and/or UL2601).

Because of the variability of designs, the above testing regimen may not be sufficient to adequately determine whether the device is substantially equivalent in safety and effectiveness to a predicate device. Consequently, additional testing may be required. Conversely, portions of the above regimen may not be applicable to every possible design configuration, thus, a justification of why certain tests were not performed may be acceptable.

E. Clinical Testing

If the intracorporeal lithotripter employs a new mechanism of action for delivering energy to the targeted stone (as compared to legally marketed devices), or has been modified to the extent where its clinical performance cannot be predicted based solely on bench testing, the sponsor should conduct a clinical study to evaluate whether the lithotripter's new technological characteristics are as safe and as effective as those of the predicate device. It is recommended that the Urology and Lithotripsy Devices Branch be contacted prior to submitting a 510(k), with any questions about the necessity of clinical data for a specific device.

If the sponsor is requesting the addition of device-specific claims regarding the clinical performance of the device, clinical data sufficient to statistically support such claims should be submitted. Consult the Urology and Lithotripsy Devices Branch for guidance on the appropriate study design to address the particular clinical performance claims proposed for the device.

Any U.S. clinical investigation of an intracorporeal lithotripter 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.

F. Sterilization

The following information regarding the device's sterilization process should be provided: (i) the method of sterilization; (ii) the method/protocol used to validate the sterilization cycle; (iii) the sterility assurance level (SAL); (iv) a description of the packaging materials; (v) the residual levels of ethylene oxide, ethylene chlorohydrin, and ethylene glycol remaining on the device after the sterilization quarantine period (if applicable); and (vi) the radiation dose (if applicable). If other sterilization methods are used, documentation should be provided to support the specific method used.

If portions of the device are supplied non-sterile and/or can be resterilized, validated sterilization instructions should be supplied in the labeling.

9. Labeling

A. General Labeling Considerations

Proposed labels, labeling, operator's manuals, and any promotional information sufficient to describe the proposed intracorporeal lithotripter, 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) and under the authority of section 515(d)(1)(B)(ii) of the 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; and (2) "Labeling: Regulatory Requirements for Medical Devices," HHS Publication FDA 89-4203. This information is available from DSMA.

B. Labeling Recommendations Specific to Intracorporeal Lithotripters

Highlighted below is additional guidance for some specific labeling recommendations for intracorporeal lithotripters.

1. Device labeling for the intracorporeal lithotripter should include the device name, corporation name, address, telephone number, the prescription device statement, intended use, single or multiple use status (for each component), and a description of the device (including dimensional specifications).

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

3. The directions for use should contain the following to inform the user about various concerns associated with using these devices:

    a. Labeling to minimize the risk of electrical energy to the patient or user. Examples of this labeling include, but are not limited to, instructions of how to properly ground the generator prior to use and how to inspect (e.g., visually) the device for signs of potential electrical safety hazard (e.g., frayed cord). Any electrical safety standards that the device conforms to should also be referenced in the manual.

    b. Labeling discussing the potential for tissue damage (e.g., perforation of the bladder or ureter, thermal damage) that exists with the device. This labeling should include, but is not limited to, a statement that the probes should not directly contact mucosal tissue.

    c. Labeling discussing the potential for the probe to break during the procedure. This labeling should include instructions for removal of the broken probe as well as informing the user that an extra probe should be available to finish the procedure. Finally, instructions informing the user how to visually inspect the probe prior to use should also be included.

    d. Labeling containing warnings that the following adverse events can occur with the device: (i) bleeding in the biliary passages and/or blood in the urine; (ii) pain; (iii) renal damage; and (iv) any other potential events (e.g., infection, events associated with endoscopy, etc.).

e. Labeling discussing the fact that the lowest effective setting should be utilized when attempting to break a stone. This statement is necessary since the use of lower settings will reduce the possibility of damage to the kidney or ureteral wall and also may reduce the possibility of propelling a stone fragment into the surrounding tissue. Imbedded fragments are problematic since they may serve as a nidus for future stone formation.

C. Patient Labeling

Patient labeling is not required for intracorporeal lithotripters. However, if patient labeling is intended to be distributed with the device, it should be submitted in the 510(k) for review. For manufacturers wishing to develop patient labeling, the following items should be considered:

- labeling should be written and formatted so as to be easily read and understood by most patients (i.e., 7th grade reading level);
- it should give readers realistic expectations of the benefits and risks of intracorporeal lithotripsy treatment, and briefly describe each of the potential complications; and
- it should briefly describe the alternative treatments.

D. Promotional Literature

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

10. 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.

11. Device Modifications

Guidance concerning the premarket requirements for device modifications is available in the document entitled "Deciding When to Submit a 510(k) for a 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*).