Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use

Document issued on: July 20, 2011

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Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to http://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Guidance for Industry and FDA Staff

Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use

1. Introduction

This guidance document was developed as a special control guidance to support the classification of the focused ultrasound stimulator system for aesthetic use into class II (special controls). The device is intended to apply focused ultrasound energy to the body to achieve temporary changes in physical appearance. This guidance document is issued in conjunction with a Federal Register notice announcing the classification of the focused ultrasound stimulator system for aesthetic use.

Following the effective date of the final rule, manufacturers of devices within this generic type of device will need to address the issues covered in the special control guidance. However, the manufacturer need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

2. Background

FDA believes that special controls, when combined with the general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of the focused ultrasound stimulator system for aesthetic use. Therefore, a manufacturer who intends to market a device of this generic type must (1) conform to the general controls of the Federal Food, Drug & Cosmetic Act (FD&C Act), including the premarket notification requirements described in 21 CFR 807 Subpart E, (2) address the specific risks to health associated with the focused ultrasound stimulator system for aesthetic use, including those identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device.

This special control guidance document identifies the classification regulation and product code for the focused ultrasound stimulator system for aesthetic use (refer to **Section 3. Scope**). Other sections of this guidance document list the risks to health FDA has identified and describe measures that, if followed by manufacturers and combined with the

general controls, will generally address the risks associated with these focused ultrasound stimulator systems and lead to a timely 510(k) review. This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87, the guidance, **Format for Traditional and Abbreviated 510(k)s**[1] and the section of CDRH's Device Advice, **Premarket Notification Submission 510(k)**.[2]

3. Scope

The scope of this document is limited to the following class II device (product code OHV) described below.

21 CFR 878.4590 Focused Ultrasound Stimulator System for Aesthetic Use

Identification. A Focused Ultrasound Stimulator System for Aesthetic Use is a device using focused ultrasound to produce localized, mechanical motion within tissues and cells for the purpose of producing either localized heating for tissue coagulation or for mechanical cellular membrane disruption intended for non-invasive aesthetic use.

Classification. Class II (special controls). The special controls are: The FDA guidance document entitled: "Guidance for Industry and Food and Drug Administration Staff; Class II Special Controls Guidance Document: Focused Ultrasound Stimulator System for Aesthetic Use."

4. Device Description

We recommend you identify your device using regulation and product code described in **Section 3. Scope** and include the following:

Device Components
We recommend you identify all components, system software, and accessories within the scope of the 510(k).

Photograph or Drawing of the Device
We recommend you provide a photograph or drawing of the device. We also recommend you provide a functional block diagram (including all accessories).

Comparison to the Predicate Device
We recommend you explain how your device and the predicate are similar, with respect to indications for use and technological characteristics.

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[1] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm

[2] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm

5. Risks to Health

In the table below, FDA has identified the risks to health generally associated with the use of the focused ultrasound stimulator system for aesthetic use addressed in this document. The measures recommended to mitigate these identified risks are given in this guidance document, as also shown in the table below. You should also conduct a risk analysis before submitting your premarket notification to identify any other risks specific to your device. We recommend the premarket notification describe the risk analysis method and include the results. If you elect to use an alternative approach to address a particular risk identified in this guidance document, or you have identified risks additional to those in the guidance, you should provide sufficient detail to support the approach you have used to address that risk.

Identified Risk	Recommended Mitigation Measures
Thermal Injury from Focused Ultrasound Exposure (Thermal Damage)	Section 6. Bench Testing Section 7. Software Validation Section 8. Animal Testing Section 9. Clinical Testing Section 11. Electromagnetic Compatibility Section 13. Labeling
Mechanical Injury from Focused Ultrasound Exposure (Cavitation or other Mechanical Damage)	Section 6. Bench Testing Section 7. Software Validation Section 8. Animal Testing Section 9. Clinical Testing Section 13. Labeling
Ocular Injury	Section 13. Labeling
Electrical Shock	Section 12. Electrical and Mechanical Safety Performance Testing Section 13. Labeling
Inflammation/Foreign Body Response	Section 10. Biocompatibility
Use Error	Section 13. Labeling

6. Bench Testing

We recommend that preclinical testing be performed to demonstrate that the focused ultrasound stimulator system for aesthetic use meets all design specification and performance requirements. In regard to acoustic power and performance, acoustic power measurements should be conducted with the data demonstrating that the radiated acoustic power is predictable and that there is low variability among transducers. Testing should accurately characterize the acoustic beam profile and establish that the acoustic energy is delivered and concentrated in the desired target location. If thermal coagulation is intended, then testing should demonstrate that the device can produce predictable thermal lesions via both measurements of temperature distributions in vitro, such as in tissue mimicking materials, and via computational modeling of the thermal dose. Testing

should demonstrate the safety of non-targeted tissues both proximal and distal to the targeted region, including bone and nerve, through in vitro acoustic and thermal measurements and computational modeling. The cooling time between exposures chosen to avoid residual temperature rise should be justified. Testing should demonstrate the accuracy of the method for targeting the region of interest and, if applicable, for monitoring the progress or result of treatment. Testing should address possible cavitation and bubble formation either in the focal region or at the device-tissue interface, means for its detection, and possible consequences regarding both safety and effectiveness.

Testing should be performed to assess the probability of system failure and the means by which system failure can be mitigated or is apparent to the user. The overall system should be tested to ensure proper performance to design specifications and to assess the failure modes and probabilities. Bench testing may also be used to assess the likelihood that the conditions of use may affect system performance.

7. Software Validation

We recommend that you submit the information for software-controlled devices described in **Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices**.[3] The kind of information we recommend you submit is determined by the "level of concern," which is related to risks associated with software failure. The level of concern for a device may be minor, moderate, or major. FDA believes that the software used to operate the device presents a "moderate level of concern" as described in the Software Guidance because a failure or latent design flaw could directly result in minor injury to the patient or operator.

In addition, we recommend that the development of the control software follow IEC 60601-1-4: Medical electrical equipment – Part 1-4; "General Requirements for Safety; Collateral Standard: Programmable electrical medical devices" or equivalent methods.

8. Animal Testing

We recommend that you evaluate the functionality and safety of the focused ultrasound stimulator system for aesthetic use under simulated use conditions using *in vivo* or *ex vivo* models as appropriate. Studies should characterize dose dependent tissue effects and permit an assessment of the probability of an inadvertent deposition of energy into distal and/or surrounding non-target tissue. In addition to mitigating the risks of an unintentional dose being delivered to non-target tissue, evidence should be provided that demonstrate that the desired tissue effects are limited to well-defined target areas with clearly evident boundaries. Testing protocols should also simulate actual use conditions and demonstrate the system's functional ability to create the desired series of treatment zones, e.g., approximately 1 mm^3 using a minimal energy exposure for 10-100 ms.

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[3] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089593.pdf

The conduct of preclinical animal studies should follow modern practices of humane care and use (please refer to **Appendix A**), including thorough veterinary medical record-keeping at all stages of the study, appropriate training of personnel, and adequate controls for the minimization of infections, pain and distress, and other experimental confounders. Standard operating procedures consistent with refinements, reductions, and where appropriate validated models exist, replacement, should also be implemented.[4] FDA also requires that animal studies to support marketing and research applications are conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR Part 58).

9. Clinical Testing

In accordance with the FD&C Act, the agency will rely upon well-designed bench and/or animal testing rather than requiring clinical studies for new devices unless there is a specific justification for asking for clinical information to support a determination of substantial equivalence. While, in general, clinical studies may not be needed for most focused ultrasound stimulator systems for aesthetic use, FDA may recommend that you collect clinical data for a focused ultrasound stimulator system for aesthetic use with any of the following:

- indications for use dissimilar from a legally marketed system of the same type;
- designs dissimilar from designs previously cleared under a premarket notification; or
- new technology, i.e., technology different from that used in legally marketed focused ultrasound stimulator systems for aesthetic use.

FDA will consider alternatives to clinical testing when the proposed alternatives are supported by an adequate scientific rationale. Also note that, as with any premarket notification, any new intended uses or technology differences that raise new types of safety or effectiveness questions may be grounds for finding your device not substantially equivalent (NSE).

If a clinical study is needed, we recommend that you evaluate the safety and effectiveness of the particular focused ultrasound stimulator system for aesthetic use demonstrating its ability to achieve the desired aesthetic results in a significant portion of the target population when used for the proposed indications for use and under the proposed conditions of use, including adequate direction for use and warnings against unsafe use that appear in the labeling. We suggest that you use any clinical studies that are

[4] ANSI/AAMI/ISO 10993-2:2006: Biological evaluation of medical devices – Part 2: Animal welfare requirements
And
Russell, W.M.S. and Burch, R.L., The Principles of Humane Experimental Technique. Methuen, London, 1959. Reprinted by UFAW, 1992: 8 Hamilton Close, South Mimms, Potters Bar, Herts EN6 3QD England. ISBN 0 900767 78 2

conducted to confirm the safety of the device that was established through bench and animal testing.

If a clinical study is needed to demonstrate substantial equivalence, i.e., conducted prior to obtaining a 510(k) clearance of the device, the study must be conducted under the Investigational Device Exemptions (IDE) regulation, 21 CFR Part 812. We believe that the system addressed by this guidance document is a significant risk device as defined in 21 CFR 812.3(m).[5] In addition to the requirement of having an FDA-approved IDE, sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

10. Biocompatibility

We recommend that you evaluate the biocompatibility of the device as described in the International Organization for Standardization (ISO) standard ISO-10993-1, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing for intermittent external contact with intact external body surfaces. If identical materials and identical material processing are used in a predicate device with the same type and duration of patient contact, you may identify the predicate device in lieu of performing biocompatibility testing.

11. Electromagnetic Compatibility (EMC)

We recommend that you demonstrate the EMC of the device by performing EMC testing as described in the following FDA-recognized standard or equivalent method.

- IEC 60601-1-2 (Second Edition, 2001) Medical Electrical Equipment – Part 1: General Requirements for Safety; Electromagnetic compatibility – Requirements and Tests.

12. Electrical and Mechanical Safety Performance Testing

We recommend that you demonstrate the electrical and mechanical safety of the device by performing electrical and mechanical safety testing as described in the following FDA-recognized standard or equivalent method.

- IEC 60601-1, Medical Electrical Equipment – Part 1: General Requirements for Safety.

[5] For additional information regarding clinical trial requirements, see Information Sheet Guidances Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors , available at: http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/default.htm

- IEC 60601-2-37:2004-08 Particular requirements for the safety of ultrasonic medical diagnostic and monitoring equipment.

13. Labeling

The premarket notification must include labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). The following suggestions are aimed at assisting you in preparing the labeling that satisfies the requirements of 21 CFR Part 801.[6]

Device User Manual
We recommend that you provide a user manual with the device. The user manual should include descriptions of:

- the device and all accessories
- how the device interconnects with other components or accessories
- all features, functions, output modalities, and specifications
- all user-accessible controls
- indicators, markings, and/or labels on the device which provide information regarding the function or meaning of each control, display output jack, etc.
- illustrations of the device and accessories

Directions for Use
As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use. Labeling must include, however, adequate information for practitioner use of the device, including indications, effects, routes, methods, frequency and duration of administration and any relevant hazards, contraindications, side effects and precautions. (21 CFR 801.109(d)).

Indications for Use
We recommend that the indications for use be included in the user manual.

Contraindications
We recommend that you advise users with open wounds or lesions, including severe or cystic acne, active implantables (e.g., pacemakers or defibrillators), or metallic implants not to use the device in these areas.

Storage Conditions
We recommend that storage conditions be included in the user manual.

Warnings

[6] Although final labeling is not required for 510(k) clearance, final labeling must comply with the requirements of 21 CFR Part 801 before a medical device is introduced into interstate commerce. In addition, final labeling for prescription medical devices must comply with 21 CFR 801.109. Labeling recommendations in this guidance are consistent with the requirements of Part 801.

Should describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur.

Should include an appropriate warning if there is reasonable evidence of an association of a serious hazard with the use of the device. A causal relationship need not have been proved.

Should include a warning to ensure complete handpiece skin contact and to not expose the eyes to ultrasound radiation.

We believe a warning is appropriate when the device is commonly used for disease or condition for which there is a lack of valid scientific evidence of effectiveness for that disease or condition and such usage is associated with a serious risk or hazard.

Precautions

Should include information regarding any special care to be exercised by the practitioner and/or patient for the safe and effective use of the device, for example:

- Should indicate or emphasize any need for protective wear during use.
- Should identify any laboratory tests or other evaluations that may be helpful in following the patient's response or identify adverse reactions and, if appropriate, specify the frequency of such tests or evaluations before, during and after use of the device.
- Should identify any precautions to help prevent electrical shock, such as any need for specific device placement, appropriate electrical wiring needs, reminders to periodically check device wiring and accessories for damage, and avoidance of use of the device in environments where electrical shock is possible.

Appendix A

As stated in Section 9, the conduct of preclinical animal studies should follow modern practices of humane care and use. All animal studies should be designed based on the modern practices described in the following references.

1. Animal Welfare Act, Code of Federal Regulations, Title 9 Volume 1, 7 USC 2131-2156
    - Definitions: http://www.access.gpo.gov/nara/cfr/waisidx_03/9cfr1_03.html
    - Regulations: http://www.access.gpo.gov/nara/cfr/waisidx_03/9cfr2_03.html
    - Standards: http://www.access.gpo.gov/nara/cfr/waisidx_03/9cfr3_03.html
    - Applicable Policies: http://www.aphis.usda.gov/animal_welfare/policy.shtml

2. Public Health Service Policy on Humane Care and Use of Laboratory Animals, Office of Protection from Research Risks, NIH, Bethesda, MD, 1996: http://grants.nih.gov/grants/olaw/references/phspol.htm

3. Public Law 99-158 "Animals in Research" Health Research Extension Act of 1985 November 20, 1985. http://grants.nih.gov/grants/olaw/references/phspol.htm#Health%20Research%20Extension%20Act%20of%201985.

4. US Government Principles for the Utilization of and Care of Vertebrate Animals Used in Testing, Research, and Training. http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples.

5. Guide for the Care and Use of Laboratory Animals. National Research Council, Institute of Laboratory Animal Resources Commission on Life Sciences 1996. National Academies of Science Press, Washington, DC. http://www.nap.edu/openbook.php?record_id=5140&page=8