Guidance for Industry and FDA Staff

Keratome and Replacement Keratome Blades Premarket Notification [510(k)] Submissions

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For questions regarding this document, contact Everette T. Beers at 301-594-2018 ext. 136 or by email at everette.beers@fda.hhs.gov.

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

Diagnostics and Surgical Devices Branch
Division of Ophthalmic, Ear, Nose and Throat Devices
Office of Device Evaluation

Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to http://www.fda.gov/dockets/ecomments. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

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Table of Contents

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

FDA has developed this guidance document to assist industry in preparing premarket notification submissions for keratomes and replacement keratome blades. The device is intended to shave tissue from sections of the cornea for a lamellar (partial thickness) transplant. Keratomes, originally used during cornea transplant surgery, are now widely used during the laser refractive surgical procedure known as laser-assisted in situ keratomileusis (LASIK).

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to follow the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency'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.

2. Background

A manufacturer who intends to market a device of this generic type should conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the act), including the premarket notification requirements described in 21 CFR 807 Subpart E, and obtain a substantial equivalence determination from FDA prior to marketing the device. (See also 21 CFR 807.81 and 807.87). This guidance document identifies the classification regulation and product codes for keratomes and replacement keratome blades (refer to **Section 4. Scope**). In addition, other sections of this guidance document provide additional information to manufacturers on addressing risks related to these devices in premarket notifications (510(k)s).

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 and "**How to Prepare a 510(k) Submission**" on FDA Device Advice at http://www.fda.gov/cdrh/devadvice/314.html.

Under "**The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications**," http://www.fda.gov/cdrh/ode/parad510.html, a manufacturer may submit a Traditional 510(k) or has the option of submitting either an Abbreviated 510(k) or a Special 510(k). FDA believes an Abbreviated 510(k) provides the least burdensome means of demonstrating substantial equivalence for a new device, particularly once FDA has issued a guidance document addressing that device. Manufacturers considering certain modifications to their own cleared devices may lessen the regulatory burden by submitting a Special 510(k).

3. The Content and Format of an Abbreviated 510(k) Submission

An Abbreviated 510(k) submission must include the required elements identified in 21 CFR 807.87, including the proposed labeling for the device sufficient to describe the device, its intended use, and the directions for its use. In an Abbreviated 510(k), FDA may consider the contents of a summary report to be appropriate supporting data within the meaning of 21 CFR 807.87(f) or (g); therefore, we recommend that you include a summary report. The report should describe how this guidance document was used during the device development and testing and should briefly describe the methods or tests used and a summary of the test data or description of the acceptance criteria applied to address the risks identified in this document, as well as any additional risks specific to your device. This section suggests information to fulfill some of the requirements of section 807.87 as well as some other items that we recommend you include in an Abbreviated 510(k).

Coversheet

The coversheet should prominently identify the submission as an Abbreviated 510(k) and cite the title of this guidance document.

Proposed labeling

Proposed labeling should be sufficient to describe the device, its intended use, and the directions for its use. (Please refer to **Section 14. Labeling** for specific information that should be included in the labeling for devices of the types covered by this guidance document.)

Summary report

We recommend that the summary report contain:

Description of the device and its intended use

We recommend that you describe the performance specifications and, when appropriate, include detailed, labeled drawings of the device. Please refer to **Section 5**. **Device Description** for specific information that we recommend you include in the device description for devices of the types covered by this guidance document. You should also submit an "indications for use" enclosure.[1]

Description of device design

We recommend that you include a brief description of the device design requirements.

Identification of the risk analysis method

We recommend that you identify the risk analysis method(s) you used to assess the risk profile, in general, as well as the specific device's design and the results of this analysis. (Please refer to **Section 6**. **Risks to Health** and **Section 7. Hazards Assessment** for the risks to health generally associated with the use of this device that FDA has identified.)

Discussion of the device characteristics

We recommend that you discuss the device characteristics that address the risks identified in this guidance document, as well as any additional risks identified in your risk analysis.

Description of the performance aspects

We recommend that you include a brief description of the test method(s) you have used or intend to use to address each performance aspect identified in **Sections 5 - 13** of this guidance document. If you follow a suggested test method, you may cite the method rather than describing it. If you modify a suggested test method, you may cite the method

[1] Refer to http://www.fda.gov/cdrh/ode/indicate.html for the recommended format.

but should provide sufficient information to explain the nature of and reason for the modification. For each test, you may either (1) briefly present the data resulting from the test in clear and concise form, such as a table, **or** (2) describe the acceptance criteria that you will apply to your test results.[2] (See also 21 CFR 820.30, Subpart C - Design Controls for the Quality System Regulation.)

Reliance on standards

If you choose to rely on a recognized standard for any part of the device design or testing, you may include either a:

- statement that testing will be conducted and meet specified acceptance criteria before the device is marketed; or
- declaration of conformity to the standard.[3]

Because a declaration of conformity is based on results from testing, we believe you cannot properly submit a declaration of conformity until you have completed the testing the standard describes. For more information, please refer to section 514(c)(1)(B) of the act and the FDA guidance, **Use of Standards in Substantial Equivalence Determinations**, http://www.fda.gov/cdrh/ode/guidance/1131.html.

If it is not clear how you have addressed the risks identified by FDA or additional risks identified through your risk analysis, we may request additional information about aspects of the device's performance characteristics. We may also request additional information if we need it to assess the adequacy of your acceptance criteria. (Under 21 CFR 807.87(l), we may request any additional information that is necessary to reach a determination regarding substantial equivalence.)

As an alternative to submitting an Abbreviated 510(k), you can submit a Traditional 510(k) that provides all of the information and data required under 21 CFR 807.87 and described in this guidance. A Traditional 510(k) should include all of your methods, data, acceptance criteria, and conclusions. Manufacturers considering certain modifications to their own cleared devices should consider submitting Special 510(k)s.

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[2] If FDA makes a substantial equivalence determination based on acceptance criteria, the subject device should be tested and shown to meet these acceptance criteria before being introduced into interstate commerce. If the finished device does not meet the acceptance criteria and, thus, differs from the device described in the cleared 510(k), FDA recommends that submitters apply the same criteria used to assess modifications to legally marketed devices (21 CFR 807.81(a)(3)) to determine whether marketing of the finished device requires clearance of a new 510(k).

[3] See **Required Elements for a Declaration of Conformity to a Recognized Standard** (Screening Checklist for All Premarket Notification [510(K)] Submissions), http://www.fda.gov/cdrh/ode/reqrecstand.html.

4. Scope

The scope of this document is limited to the device described below, 21 CFR 886.4370, class I, product codes HNO (Keratome, AC-Powered), HMY (Keratome, Battery-Powered), and NKY (Blade, Keratome, Reprocessed).

> **§ 21 CFR 886.4370 Keratome.**
>
> A keratome is an AC-powered or battery powered device intended to shave tissue from sections of the cornea for a lamellar (partial thickness) transplant.

Water jet keratomes (product code MYD) classified under 886.4370 are not within the scope of this guidance. Laser keratome devices classified under 21 CFR 878.4810, Laser Surgical Instrument for Use in General and Plastic Surgery and in Dermatology also are not within the scope of this guidance. In addition, reprocessed single use devices—such as reprocessed keratome blades—have additional requirements for validation of the cleaning and sterilization process that are not discussed in this guidance.[4]

5. Device Description

We recommend that you identify your device by the regulation and product code described in **Section 4.** We recommend that you provide a description, as discussed below, of the technical specifications, principles of operation, and of any keratome blades used with your device.

A. Technical Specifications

1. We recommend you list, with references to drawings or photographs, all parts (and associated specifications) necessary to carry out the device's intended use, including, but not limited to:
   - console, handpiece, motors, keratome head, keratome blades, tubing, fixation ring, eye attachment mechanism;
   - any interchangeable components used to change depth or diameter of the flap or width of the hinge (e.g., depth plates); and
   - any items that can be ordered as optional add-ons.

2. We recommend you identify the material composition of device components and include references to your drawings or photographs.

[4] See Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html.

3. We recommend you provide a physical description of the device (e.g., size, weight, dimensions) with legible dimensional drawings.

B. Principles of Operation

We recommend you describe the method of operation, including, but not limited to, the information described below.

1. The means by which the blade moves across the cornea to perform a cut, the:
    - advancement rate of the blade (mm/sec)
    - oscillation rate of the blade (rpm)
    - manual, electric (AC or DC), or pneumatic motor, and specifications
    - use of rails, gears, etc.
    - description of any other movement of the blade.

2. A description of the cut produced, including the:
    - type of hinge or flap (nasal or superior)
    - methods and components used to produce variable hinge, diameter, or thickness, if appropriate
    - nominal flap thickness(es)
    - nominal flap diameter(s)
    - nominal hinge widths(s).

3. The means by which the blade is halted for the creation of a hinge or flap (e.g., a mechanical stop or software control).

4. The means by which the keratome attaches to the cornea (e.g., a vacuum fixation ring), the vacuum produced, and the maximum intraocular pressure (IOP) achieved during fixation.

5. Any diagrams and pictures that illustrate the points above.

C. Keratome Blade

We recommend you include a description of the keratome blade and blade holder, including, but not limited to:

1. An engineering drawing of the blade that includes the dimensions and tolerances of the blade (including width, length, thickness, and bevels), blade holder (if applicable), and the mounting holes in the blade (if applicable).

2. A complete description of the materials in the blade (e.g., types and grades) and in the blade holder that includes any applicable ASTM standards.

3. The identity of any residue (e.g., oils) remaining on the blade due to the manufacturing process.

4. The hardness and sharpness of the blade with a description of the tests employed to measure each.

6. Risks to Health

In the table below, FDA has identified the risks to health generally associated with the use of the keratome and the keratome blades addressed in this document. The measures recommended to mitigate these identified risks are given in this guidance document, as shown in the table below. We recommend that you conduct a risk analysis to identify any other risks specific to your device and include the results of this analysis. The 510(k) should also describe the risk analysis method used. If you elect to use an alternative approach to address a particular risk identified in this document, or have identified risks additional to those in this document, you should provide sufficient detail to support the approach you have used to address that risk.

Identified Risk	Recommended Mitigation Measures
Inadequate Performance	Section 7. Preclinical assessment Section 8. Software assessment Section 12. Labeling
Inflammation and Infection (e.g., keratitis, epithelial ingrowth, debris in the interface)	Section 10. Material Characterization and Biocompatibility Section 11. Validation of Cleaning and Sterilization Section 12. Labeling
Electrical shock	Section 9. Electrical Safety Assessment

7. Preclinical Assessment

We recommend you provide data from validation testing of your keratome. This testing should address the accuracy, precision, and quality of the corneal flaps produced by your device, as well as the overall design of the device at a system level.

A. Validation of Cut

We recommend you provide the mean flap thicknesses, flap diameters, and hinge widths when the keratome is used in a statistically justifiable number of pig or cadaver eyes (e.g., 30 eyes per diameter and thickness). We recommend you test all the combinations of flap thicknesses, flap diameters, and hinge widths. We also recommend you provide data showing the nominal values, mean values, repeatability limits (i.e., the variability associated with cuts on a series of eyes using the same device and operator), and reproducibility limits (i.e., the variability associated with several series of eyes using different devices and operators) for all measured quantities. A tabular format of this data is desirable. We recommend you fully describe all associated test methods. We also recommend you provide general comments on your results, specifically addressing:

- the quality of the stromal bed produced (smooth, saw tooth, rough or other appropriate description)
- quality of the flap produced
- any significant differences between the nominal and measured values, wide variances or outliers, if present
- any anomalies noticed during the testing or in the data
- why you believe the flaps, hinges and stromal beds produced by your device are clinically acceptable.

If the device is an epikeratome, we recommend you also perform testing to determine the percentage of successful flaps (i.e., no residual patches of epithelium and an intact flap), percentage of partial cuts, percentage of torn flaps, and percentage of eyes with cellular debris requiring additional scraping. (Note that flap thickness testing is not recommended for epikeratomes, but flap diameters and hinge widths should be validated as described above.) We recommend you fully describe all associated test methods and provide general comments on your results. Specifically, we recommend that your comments explain why the rates of unsuccessful flaps, partial cuts, torn flaps, and cellular debris you observe are clinically acceptable.

You may include any available clinical data to support the validation information recommended above for keratomes and epikeratomes.

B. Validation of Device Design

We recommend you conduct system level validation testing to ensure all hardware and software systems in the device are functioning properly. We recommend you validate all alarms and warnings (e.g., warnings or alarms for insufficient vacuum or improper assembly) under realistic fault conditions. For more details on software validation, please refer to Section 8 below.

8. Software Validation

Manufacturers of class I devices automated with computer software must comply with the requirements of Design Controls (21 CFR 820.30, Subpart C) under the Quality System Regulations, 21 CFR 820.30(a)(2)(i). In accordance with these requirements, you must perform design validation, which includes a software validation and risk analysis, where appropriate, and document the design validation results in your design history file as described under 21 CFR 820.30(g).

Please refer to the Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, http://www.fda.gov/cdrh/ode/guidance/337.html, for a discussion of the software documentation that you should provide. Please also refer to the General Principles of Software Validation, http://www.fda.gov/cdrh/comp/guidance/938.html, for a discussion of general principles that the FDA considers applicable to the validation of medical device software.

We encourage you to take advantage of any recognized software standards and provide statements or declarations of conformity as described in the FDA guidance, **Use of Standards in Substantial Equivalence Determinations**, http://www.fda.gov/cdrh/ode/guidance/1131.html. Please visit the following website to search for the standards that have been recognized when a medical device contains software, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm.

9. Electrical Safety and Electromagnetic Compatibility

We recommend you address the electrical safety and electromagnetic compatibility of your device by following both standards below or equivalent methods:

- International Electrotechnical Committee (IEC) standard IEC 60601-1, Medical Electrical Equipment Part 1: General Requirements for Safety
- IEC 60601-1, Part 1-2: General Requirements for Safety - Collateral Standard: Electromagnetic Compatibility - Requirements and Tests

Electromagnetic compatibility (EMC) encompasses both emissions (interference with other electronic devices) and immunity (interference with device performance created by emissions from other electronic devices). We recommend you evaluate the EMC of your device as discussed below.

Emissions

EMC testing should demonstrate that the device will not adversely interfere with the performance of other electronic devices (*emissions*). Testing should include radio frequency (RF) electromagnetic, low frequency magnetic, and conducted emissions testing.

Immunity

EMC testing should also demonstrate that the device will perform as expected in the presence of other electrical and electronic devices or other sources of electromagnetic disturbance (EMD) in the intended environment of use (*immunity*). The device should operate in an acceptable manner (few EMC standards require operation within specification) during and after exposure to various forms of electromagnetic disturbance. Testing should include:

- electrostatic discharge (ESD)
- radiated RF electromagnetic fields
- electrical fast transient and bursts
- surges
- conducted RF electromagnetic energy
- voltage dips, short interruptions, and voltage variations on power supply input lines
- low- frequency magnetic fields
- quasi-static electric fields.

We recommend that you test your device according to IEC 60601-1-2 Medical Electrical Equipment – Part 1: General Requirements for Safety; Electromagnetic Compatibility – Requirements and Tests (Second Edition, 2001) to demonstrate the EMC characteristics of your device.

10. Material Characterization and Biocompatibility

FDA recommends you conduct biocompatibility testing as described in the FDA guidance, **Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing (**the Biocompatibility guidance).[5] We consider keratome blades as devices with limited contact with breached or compromised surfaces. We recommend you select biocompatibility tests appropriate for the duration and level of contact with your device. You should prepare samples for biocompatibility testing in a way that reflects the actual conditions of use (e.g., if the material will be heated during use, it should be heated to adequate temperature prior to testing). If identical materials and identical material processing are used in a predicate

[5] http://www.fda.gov/cdrh/g951.html

device with the same type and duration of patient contact, you may identify the predicate device in lieu of providing biocompatibility testing.

11. Sterilization

For single use devices that are provided sterile, we recommend you provide sterilization information described in the guidance entitled, **Updated 510(k) Sterility Review Guidance K90-1**.[6] The device should be sterile with a sterility assurance level (SAL) of 1×10^{-6} using a sterilization cycle validated in accordance with the Quality System Regulation (QSR) 21 CFR Part 820. In addition, we recommend you provide a description of the packaging that maintains the device's sterility.

If the device is reusable, we recommend you identify the method that you used to validate the cleaning, disinfection, and sterilization of your device. (See also **Section 12. Labeling**.) In addition, we recommend you specify any limit on the number of times re-sterilization and reuse can be done without adversely affecting the safety, effectiveness, or performance of the device.

12. Labeling

The premarket notification must include labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). The following suggestions are intended to assist you in preparing labeling that satisfies the requirements of 21 CFR Part 801.[7]

Directions for use

As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use. Nevertheless, under 21 CFR 807.87(e), we recommend providing clear and concise instructions that delineate the technological features of the specific device and how the device is to be used on patients. Instructions should encourage local/institutional training programs designed to familiarize users with the features of the device and how to use the device in a safe and effective manner.

The user's manual should include instructions for cleaning and sterilization procedures, if appropriate.

Your labeling should include indications for use, for example:

> A keratome is indicated for cutting the cornea prior to lamellar (partial thickness) transplant or to create a flap in the cornea prior to LASIK surgery or prior to another procedure requiring a corneal flap.

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[6] http://www.fda.gov/cdrh/ode/guidance/361.html.

[7] 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.

We also recommend that you include the nominal values, mean values, repeatability limits, and reproducibility limits for flap thickness, flap diameter, and hinge width in the user's manual. You should also include the basic details about the study design (e.g., porcine or human eyes, sample size) used to determine these values.

Appendix – Information for Replacement Keratome Blades

A. For each keratome, for which your blades are intended for use, we recommend you provide the:

- name of the keratome original equipment manufacturer (OEM)
- model of the keratome
- 510(k) number (if known) for each keratome.

B. We recommend you include a side-by-side comparison for each of your blades with each keratome's OEM blade. We also recommend you address the following parameters for each of your blades and the OEM blades. For each comparison and each parameter in each comparison, we recommend you comment on the similarities between blades and explain the impact on blade performance of any differences you observe. We also recommend presenting each comparison clearly and separately; a tabular format is desirable.

1. Dimensions

   We recommend you include a diagram (drawing or manufacturing blue print) of the device that illustrates the dimensions you have measured. We recommend you also include a key to the diagram (a tabular format is desirable) that shows the dimensions and tolerances for your device (blade, blade holder, keratome head, as appropriate).

   We recommend you provide all of the measurements (mean, standard deviation, and measurement precision for each) of the blade (length, width, thickness, and bevels), blade holder (if applicable), mounting holes in blade (if applicable), keratome head (if applicable), and any other specifications to compare your device and the OEM blades. We also recommend you measure a statistically justifiable number of your blades and the OEM blades, for example 30 blades.

2. Materials

   We recommend you identify and compare (by ASTM standard, specification, type, grade, certificate of analysis, etc.) the materials in the final product of your blade and the OEM blade: the blade, blade holder (if applicable), and coatings on the blade (if applicable). We also recommend you identify any remaining substances on the blade due to polishing or sharpening.

3. Hardness

   We recommend you compare the hardness of the blade and the OEM blade and indicate the test used to measure the hardness.

4. Sharpness

   We also recommend you compare the sharpness of your blade and the OEM blade and indicate the test used to measure the sharpness. Testing may combine photomicrographs and validation testing, or be stand-alone sharpness tests.

C. Preclinical Assessment: See **Section 7. Preclinical Assessment**. We also recommend you provide documentation of validation testing demonstrating the equivalency of your blade to the OEM. For each comparison and each parameter in each comparison, we recommend you comment on the similarities between the blades and explain the impact of any differences you observe on the blade performance.

D. Sterilization: See **Section 11. Sterilization**.

E. Labeling: See **Section 12. Labeling**. Labeling should include an indications for use that identifies the OEM manufacturers and model numbers your blades are intended for use with.

F. FDA recommends that manufacturers of replacement keratome blades include the accuracy, repeatability, and reproducibility information for all combinations of flap thickness, flap diameter, and hinge width compatible with the OEM keratome in the package labeling.