Guidance for Industry and FDA Staff

Tonometers - Premarket Notification [510(k)] Submissions

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Food and Drug Administration
Center for Devices and Radiological Health

Diagnostic and Surgical Devices Branch
Division of Ophthalmic and 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 Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. 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.

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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 contact and non-contact tonometers. The device is intended for measuring intraocular pressure (IOP).

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 tonometers (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; Final Guidance**," 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).

A. Coversheet

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

B. Proposed labeling

Proposed labeling should be sufficient to describe the device, its intended use, and the directions for its use. (Please refer to **Section 12. Labeling** for specific information that should be included in the labeling for devices of the type covered by this guidance document.)

C. 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 type 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** 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 7-11** 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; Final Guidance for Industry and FDA**.[4]

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] See http://www.fda.gov/cdrh/ode/guidance/1131.html

The following is a specific discussion of how you should apply this guidance document to a premarket notification submission for a tonometer.

4. Scope

The scope of this guidance document is limited to the device described below, 21 CFR 886.1930, product codes, HKY (Tonometer, Manual) and HKX (Tonometer, AC-Powered).

> **§ 21 CFR 886.1930 Tonometer and accessories.**
>
> A tonometer and accessories is a manual device intended to measure intraocular pressure by applying a known force on the globe of the eye and measuring the amount of indentation (Schiotz type) or to measure intraocular tension by applanation (applying a small flat disk to the cornea). Accessories for the device may include a tonometer calibrator or a tonograph recording system. The device is intended for use in the diagnosis of glaucoma.

The generic type device includes other types of contact tonometers (e.g., strain gauge), as well as non-contact (i.e., air-puff) tonometers. It also encompasses tonometers that adjust IOP based on other ocular parameters. These technologies are within the scope of this guidance.

5. Device Description

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

A. Principles of Operation

1. Measurement Method

We recommend you describe the parameters used to measure IOP and any other quantities measured by the device, such as corneal mechanical properties and corneal geometry, if applicable.

2. Signal Processing

We recommend that you provide the main signal processing and computational steps involved in converting a raw signal into an IOP reading and other quantities, if applicable.

3. Calibration

We recommend that you provide how the device is calibrated during production and how calibration is maintained over the life of the device.

4. Adjustments to IOP

If the device adjusts measured IOP based on other ocular parameters (e.g., corneal thickness or mechanical properties), we recommend that you explain the scientific basis for these adjustments, including appropriate theoretical and empirical analyses (see **Sections 7**-**8**). We also recommend that you submit any relevant literature references.

B. Technical Specifications

In describing the technical specifications of your device, we recommend that you include:

- measurement range
- accuracy (e.g., 95% tolerance interval relative to manometry) and repeatability (e.g., coefficient of variation)
- applanation area, contact area, or area of corneal deformation
- type of pressure transducer (e.g., optical detector, strain gauge) and specifications
- electrical specifications
- data display and output type (e.g., numerical digital, computer screen, printout)
- data storage capability (e.g., measurement results, patient information)
- interface with other equipment (e.g., printer, computer network)
- dimensions and weight.

6. Risks to Health

In the table below, FDA has identified the risks to health generally associated with the use of the device 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 also conduct a risk analysis, prior to submitting your 510(k), to identify any other risks specific to your device and submit the results of this analysis. 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, then you should provide sufficient detail to support the approach you have used to address that risk.

Identified Risk	Recommended Mitigation Measures
Inaccurate or unreliable measurement and consequent inappropriate therapy	Section 7. Bench Testing Section 8. Clinical Performance Section 12. Labeling
Infection	Section 9. Validation of Cleaning and Sterilization Methods
Tissue adverse reaction	Section 10. Biocompatibility
Electrical shock or electromagnetic interference	Section 11. Electrical Safety and Electromagnetic Compatibility

7. Bench Testing

For all tonometers, we recommend that you provide accuracy and repeatability results for your device that span the nominal range of pressures your device is intended to measure. This testing may be an element of a clinical study; or it may be accomplished through use of pressure-controlled model, *ex vivo* animal, or human (eye bank) eyes.

For any method used, we recommend that you describe its strengths and limitations. We also recommend that you validate your baseline IOP during testing and verify that the act of repeated measurements does not significantly influence IOP.

A. Accuracy

If you use pressure-controlled eyes (i.e., model, animal, or eye bank eyes) in your accuracy studies, we recommend that you conduct testing at the lower limit of the nominal pressure measurement range and every multiple of 10 mmHg, up to the upper limit. For a device with a nominal range of 5 to 45 mmHg, for example, we recommend that you test at 5, 10, 20, 30, 40, and 45 mmHg.

B. Repeatability

We recommend that you conduct testing on a set of 3 (or more) eyes for each pressure value, with 10 measurements (i.e., normal clinical outputs) per eye. Each eye should only be used at one pressure.

We recommend that for each eye at each reference pressure, you report the mean measured IOP, standard deviation, and coefficient of variation. Additionally, we recommend that you

report the overall accuracy and repeatability at each pressure as the average of the 3 (or more) mean measured IOP values and the average of the 3 (or more) coefficients of variation at that pressure.

C. Additional Device Features

If the device contains any feature that adjusts the measured IOP based on other ocular parameters (e.g., corneal thickness or mechanical properties), we also recommend that you provide performance results to validate each feature.

D. Devices Containing Software

If your device contains software, we recommend you provide the information appropriate to the "level of concern" for your device, as described in **Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices**.[5]

8. Clinical Performance (non-Goldmann-type Tonometers only)

A. Non-Goldmann-type Tonometers

In addition to the bench testing described above, for all non-Goldmann-type tonometers, we recommend that you compare your device with a calibrated Goldmann-type applanation tonometer in a statistically significant representative sample of human subject's eyes.

1. Data Collection

We recommend that you follow the data collection aspects of the American National Standards Institute (ANSI) tonometer standard Z80.10-2003 or equivalent method.

2. Calibration

We recommend that you describe the calibration method and provide calibration results for the reference Goldmann-type tonometer.

3. Sample Size

We recommend a sample size of 150 eyes, distributed according to the ANSI Z80.10-2003 standard. However, we will consider an alternative sample size, if supported by a valid sample size estimate.

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

4. Testing Protocol

We recommend that your testing protocol follow Annex A.3 and Annex B, of ANSI Z80.10-2003 or equivalent method. If you use a different protocol, we recommend you provide a complete description. However, if you followed any portions of ANSI Z80.10-2003, we recommend you indicate which ones.

5. Analysis of Results

We recommend that you analyze your results as described below.

a. Scatter Plot of Measured IOP Values

We recommend that you submit a scatter plot showing the IOP values measured by your tonometer on the y-axis versus the Goldmann type tonometer on the x-axis. We also recommend that you submit a linear regression of the scatter plot data, showing the resulting line, its equation, and the correlation coefficient.

b. Bland-Altman type plot

We recommend that you submit a Bland-Altman type plot showing the paired differences between the reference Goldmann-type tonometer and your tonometer readings (y-axis) versus the mean of the Goldmann-type tonometer and your tonometer readings (x-axis).

We also recommend that you provide the mean and standard deviation of the paired differences, and show the mean and two standard deviations around it as horizontal lines on the plot. If you make multiple measurements on the same eye with either the Goldmann-type or your tonometer, we recommend that you use the mean of the normal clinical outputs of the tonometer in your analysis.

c. Comparability to a Goldmann-type Tonometer

We recommend that you tabulate the number and percent of paired differences, i.e., **[**reference tonometer measurement**] – [**your device measurement**]** that exceed the tolerance for each pressure range as described in ANSI Z80.10-2003 or equivalent method.

To show comparability to the Goldmann-type tonometer, no more than 5% of the paired differences should exceed the tolerance for each pressure range. If more than 5% of paired differences in your study exceed the tolerance, we recommend that you explain these results and provide a scientifically sound rationale for the equivalence of your device.

FDA believes the devices addressed by this guidance document is a non-significant risk device, therefore the study is subject to the abbreviated requirements of 21 CFR 812.2(b).[6] In addition to the requirements of section 21 CFR 812.2(b), sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

9. Validation of Cleaning and Sterilization Methods

For single use devices that are provided sterile, 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). We also recommend you provide the sterilization information described in the guidance entitled, **Updated 510(k) Sterility Review Guidance K90-1**.[7]

For tip covers, we recommend high-level disinfection or sterilization before use.

If the device is reusable, we recommend that you identify the method that you used to validate the cleaning, disinfection, and sterilization of your device. (See also **Section 12. Labeling**.)

10. Biocompatibility

We recommend that you evaluate the biocompatibility of the patient-contacting materials as described in the **International Standard Organization (ISO) standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing**,[8] for limited contact with intact corneas. 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. We also recommend that you provide a list of the patient-contacting materials in your device.

11. Electrical Safety and Electromagnetic Compatibility

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

- 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

[6] See http://www.fda.gov/oc/ohrt/irbs/devices.html#risk
[7] http://www.fda.gov/cdrh/ode/guidance/361.html.
[8] http://www.fda.gov/cdrh/g951.html.

12. Labeling

The premarket notification should 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 labeling that satisfies the requirements of 21 CFR Part 801.[9]

As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use. Nevertheless, 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 it in a safe and effective manner.

Labeling should include the indications for use of your device, for example:

> A tonometer is indicated for measuring intraocular pressure to aid in the screening and diagnosis of glaucoma.

Labeling should contain a summary of all performance testing of the device as outlined in **Sections 7** and **8**, including accuracy and repeatability statistics and, if applicable, comparability testing to a Goldmann-type reference tonometer. Additionally, we recommend that you include in the labeling any relevant references that describe the scientific basis for any features that adjust measured IOP.

Labeling should list separately single use, disposable, and reusable parts.

If the end user is to sterilize any parts, we also recommend that your labeling include instructions for cleaning, disinfection, and sterilization based on the validation process described in your submission. Sterilization instructions should be sufficient to achieve a sterility assurance level (SAL) of 1×10^{-6}.

[9] 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.