FDA U.S. FOOD & DRUG ADMINISTRATION

Introduction and Regulatory Reference Sheet Ophthalmic Devices Panel

Classification of Ophthalmic Dispensers

November 10, 2022

On November 10, 2022, the Ophthalmic Devices Panel (the Panel) will discuss and make recommendations regarding the classification of ophthalmic dispensers.

This device type is a pre-amendments, unclassified device, meaning that this device type was marketed prior to the Medical Device Amendments of 1976, but was not classified by the original classification panels. As a result, these devices may proceed to market via the premarket notification [510(k)] process until such time as the classification steps are completed.

FDA classifies these devices after the Agency takes the following steps: (1) receives a recommendation from a device classification panel (the Panel); (2) publishes the Panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) publishes a final regulation classifying the device.

At this meeting, the Panel will be asked to discuss the classification of ophthalmic dispensers. The Panel will discuss the cleared indications for use, the risks to health, and the available safety and effectiveness information. After this advisory panel meeting, the FDA will consider all available scientific evidence and the input from panel members in determining whether to require PMA applications for this device type, or whether this device type should be classified into Class III, Class II or Class I. The FDA will then publish a proposed rule, which will be open for a public comment period. After consideration of all additional comments received in response to the proposed rule, the FDA will proceed with issuance of a final rule, which will identify the FDA's final classification for this device type.

What is a pre-Amendments device?

The term "pre-Amendments device" refers to devices legally marketed in the U.S. by a firm before May 28, 1976 and which have not been:

- significantly changed or modified since then; and
- for which a regulation requiring a premarket approval (PMA) application has not been published by FDA.

Devices meeting the above criteria are referred to as "grandfathered" devices and do not require a 510(k). The device must have the same intended use as that marketed before May 28, 1976. If the device is labeled for a new intended use, or if the device is significantly changed or modified, then the device is considered a new device and a 510(k) must be submitted to

FDA for marketing clearance.

In order for a firm to claim that a device is a pre-amendments device, it must demonstrate that the device was labeled, promoted, and distributed in interstate commerce for a specific intended use and that intended use has not changed.

Most pre-amendments devices were classified during the original classification panels.

What is an unclassified device?

An unclassified device is a device that was marketed prior to the Medical Device Amendments of 1976 (i.e., pre-Amendments device), but was not classified by the original classification panels. Therefore, no classification regulation currently exists for this device type. Like pre- amendments devices, an unclassified device may proceed to market via the 510(k) process until such time as the classification steps are completed.

What data should be considered when making a classification recommendation?

Initial classification and reclassification decisions are based on existing information for legally marketed devices and their predicates. Although information on future technology or new indications applicable for these devices may be available, this information is not relevant to the deliberations of the Panel. The Panel must consider only the legally marketed cohort of each device type.

What are the definitions of Class I, Class II and Class III?

Federal law (Federal Food, Drug, and Cosmetic Act, section 513), established the risk-based device classification system for medical devices. Each device is assigned to one of three regulatory classes: Class I, Class II, or Class III, based on the level of control necessary to provide reasonable assurance of its safety and effectiveness.

As device class increases from Class I to Class II to Class III, the regulatory controls also increase, with Class I devices subject to the least regulatory control, and Class III devices subject to the most stringent regulatory control.

The regulatory controls for each device class include:

- Class I (low to moderate risk): General Controls
- Class II (moderate to high risk): General Controls and Special Controls
- Class III (high risk): General Controls and Premarket Approval

(PMA) Class I, General Controls

A device is Class I if general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device. Examples of general controls are: registration and

listing, medical device reporting, labeling and good manufacturing practices (GMPs). Devices may also be considered Class I if the device "is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and does not present a potential unreasonable risk of illness or injury."[1] Most Class I devices are exempt from submitting a 510(k) and can be marketed without a premarket submission. Examples of Class I devices include ophthalmic retractors, visual acuity charts, stereoscopes and keratoscopes.

Class II, Special Controls

A Class II device is "a device which cannot be classified as a Class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance."[2] Examples of special controls are: performance standards, postmarket surveillance, patient registries, and special labeling requirements. Special controls may also include specific types of performance testing (e.g., biocompatibility, sterility, electromagnetic compatibility, pre-clinical testing), which FDA may outline in the regulation. Most Class II devices require clearance of a 510(k) prior to marketing. Sponsors are required to submit valid scientific evidence in their 510(k) demonstrating that the device is as safe and effective as a predicate device. Companies submitting a 510(k) for a device must demonstrate how any specified special controls have been met in order to receive marketing clearance. Examples of Class II devices include daily wear soft contact lens (for vision correction only), optical coherence tomographer, and corneal electrodes.

Class III, Premarket Approval

A Class III device is a device which:

1. "cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device," **and**
2. "cannot be classified as a class II device because insufficient information exists to determine that the special controls…would provide reasonable assurance of its safety and effectiveness," **and**
3. "is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health," **or**
4. "presents a potential unreasonable risk of illness or injury."[3]

Class III devices require premarket approval prior to marketing the device and must provide

[1] See Section 513(a)(1)(A) of the Federal Food, Drug, and Cosmetic (FD&C) Act.
[2] See Section 513(a)(1)(B) of the FD&C Act.
[3] See Section 513(a)(1)(C) of the FD&C Act.

valid scientific evidence to demonstrate that the device has demonstrated a reasonable assurance of safety and effectiveness through the submission of a PMA application. Examples of Class III devices include intraocular lens and excimer laser systems.

What will the Panel be asked to consider in determining which device class to recommend?

Risks to Health

The FDA will present the risks to health that they have identified to be associated with use of this device type. The Panel will be asked to comment on whether they disagree with inclusion of any of the identified risks or whether they believe any other risks should be considered for this device type.

Safety and Effectiveness

The FDA will present available information regarding the safety and effectiveness of this device type as it relates to the indications for use and technology. The Panel will be asked to comment on the adequacy of the available scientific evidence with respect to safety and effectiveness for this device type and to determine whether the probable benefits to health from use of the device for the specific indications outweigh the probable risks. If safety and/or effectiveness are not established for this device type, or for specific indications or technology of this device type, PMAs should be required to establish safety and effectiveness.

Special Controls

The Panel will be asked to comment on whether any special controls can be identified to provide a reasonable assurance of safety and effectiveness in light of the available scientific evidence. If special controls can mitigate the identified risks to health, and safety and effectiveness have been established, it would be appropriate to recommend that the device type be classified into Class II, special controls.

What is a "reasonable assurance of safety"?

As defined in 21 CFR 860.7(d)(1), "There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use."

What is a "reasonable assurance of effectiveness"?

As defined in 21 CFR 860.7(e)(1), "There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results."

What are the practical implications of classifying this device type in Class III?

If FDA issues a final rule classifying ophthalmic dispensers into Class III, companies wishing to continue to market existing devices of this type must file a premarket approval (PMA) application within the specified timeframe that is designated in the final classification rule. To support approval, the information in the PMA (including clinical data) would have to demonstrate a reasonable assurance of safety and effectiveness. New devices or changes to existing devices would require approval of a PMA or PMA supplement. If a company does not file a PMA within the specified timeframe or otherwise does not receive an approval order for their product, the products are considered to be misbranded and should be removed from the market.

What happens if FDA decides to classify this device type into Class II?

If these devices are classified into Class II, these devices would continue to be subject to the premarket notification [510(k)] requirements and any special controls specified in the final classification rule. Companies with existing legally marketed devices would be subject to the newly-defined special controls and must ensure that their existing products meet all specified requirements. New devices and changes to existing devices that require a new submission to FDA would require a 510(k), demonstration that the special controls have been met, and a substantial equivalence (SE) determination.

What are the practical differences between PMA (Class III) and 510(k) (Class II) requirements?

A PMA application must provide all evidence to independently demonstrate a reasonable assurance of safety and effectiveness of the device. PMAs typically involve data from clinical trials of the specific device that support both safety and effectiveness, as well as detailed manufacturing information for the device. Conversely, a 510(k) submission can leverage existing information on predicate devices, including applicable clinical data, to support marketing clearance. For devices subject to 510(k), the premarket submission need only provide evidence that the device has indications and technological characteristics consistent with existing legally marketed predicate devices and meets any required special controls.

Once a PMA is approved, the PMA holder must report all design, manufacturing, and

labeling changes made to the approved device to FDA via PMA supplements[4] and PMA annual reports[5]. PMA holders are also typically subject to ongoing postmarket requirements. 510(k) holders are not subject to as stringent postmarket oversight. For example, for 510(k) devices, companies do not need to submit many types of minor changes to a device or its labeling to FDA for review nor do they need to submit manufacturing changes or annual reports.

Regardless of the classification of this device type, FDA does not regulate the practice of medicine, specifically, which devices clinicians can use and how they use them.

May I recommend a final classification of Class I or Class II, even if the device is eligible for Class III?

Although a device may be eligible for classification as a Class III device, you may still find that there is sufficient information (valid scientific evidence) to determine that general controls alone (Class I), or general controls and the application of special controls (Class II), can provide reasonable assurance of safety and effectiveness of the device. If this is the case, then you may recommend that the device be classified into a class other than Class III. In this scenario, then you should provide a rationale that summarizes the valid scientific evidence supporting your recommendation and identifies the controls you believe are sufficient to provide reasonable assurance of safety and effectiveness.

[4] Refer to FDA's Guidance for Industry and FDA Staff: 30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/30-day-notices-135-day-premarket-approval-pma-supplements-and-75-day-humanitarian-device-exemption).

[5] Refer to FDA's Guidance for Annual Reports for Approved Premarket Approval Applications (PMA) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/annual-reports-approved-premarket-approval-applications-pma).