CLINICAL TRIALS

BREAKING INTO THE MEDICAL DEVICE INDUSTRY

Product development pathways for devices in the United States.

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The Center for Devices and Radiological Health has been actively engaging both industry and clinicians to solicit their feedback on important labeling changes and safety requirements surrounding many of the up-and-coming products in the ophthalmic space (eg, devices for microinvasive glaucoma surgery, premium IOLs). Clinicians and industry members face unique challenges as they design product development programs and adapt to the FDA's refined expectations.

The purpose of the new "Clinical Trials" column is to highlight the various aspects of the clinical trial process in the context of a changing landscape of US and international regulation. Topics will include the importance of ambulatory surgical centers, the evolution of safety endpoints, and protocol deviations. This article focuses on the product development pathways for devices in the United States.

CLASSIFICATION OF OPHTHALMIC MEDICAL DEVICES

Typically, the FDA considers anything that is not a drug or a biologic product to be a medical device. If a product's primary intended use is achieved through chemical action or metabolism, it is usually a drug.

Medical devices are divided into three classes according to their degree of risk: the higher the class, the greater the risk and degree of regulation. Classification is also based on the device's indications for use and will determine the type of premarketing strategy required for FDA clearance/approval.[1] All devices are subject to general controls that require products to be adequately packaged and properly labeled, suitable for their intended use, manufactured under a quality control system, and listed with the FDA.[2]

Class I devices require the least regulatory control, because they are low risk and tend to be simpler in design than both other classes.[3] Ophthalmic hooks and knives, the visual acuity chart, and topographers are often listed as class I devices. Class II devices are moderate-risk devices for which general controls alone are insufficient to ensure safety and effectiveness. These products must also comply with special controls, which include labeling requirements and mandatory performance standards. Biomicroscopes, retinoscopes, AC-powered magnets, and eye-movement monitors are examples of class II devices. Because class III devices are considered high risk, their regulation is the most rigorous. These products include many implants, products that are life supporting, and other diagnostic or treatment devices that pose a substantial risk of illness or injury.[3,4] IOLs and rigid gas permeable extended-wear contact lenses are examples of class III ophthalmic devices. Generally speaking, class III devices require premarket approval (PMA), including extensive safety and effectiveness data in humans.

THE 510(K), DE NOVO, AND PMA PROCESSES

Most class II and III devices enter the market through one of two pathways: a 510(k) notification by demonstrating substantial equivalence to a previously cleared or legally marketed "predicate" device or a PMA by demonstrating safety and effectiveness.

Some devices, including most class I devices and some class II devices, are exempt from both the PMA and 510(k) processes, and others may achieve marketing authorization through the de novo process. To be cleared through the 510(k) process, a device must be considered to be as safe and effective as (ie, substantially equivalent to) a predicate device.[3] Devices are considered to be substantially equivalent if they have either

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the same intended use and materials as a predicate device or have the same intended use but are manufactured with different materials yet still present with a similar safety and efficacy profile.[3] To establish substantial equivalence, companies submitting 510(k) applications need to compare and contrast the new product with predicate devices, proof that is most often gathered through preclinical testing.

The de novo classification process is for medical devices that carry a low to moderate risk but have been labeled class III because no predicate exists.[4] If a novel device is deemed not substantially equivalent after a 510(k) submission, the submitter may put forward a de novo petition within 30 days requesting that the FDA make a risk-based assessment of the device.[4] Should the de novo petition be granted, the device can be reclassified as class I or II and be used as a predicate for future 510(k) submissions.

PMA, as opposed to 510(k) clearance, is reserved for class III devices. These applications almost always involve clinical data to support claims made about the device. To conduct a clinical study with an investigational device, an investigational device exemption must be submitted. An investigational device exemption clears a product to become part of an FDA-sanctioned clinical study and is parallel to an investigational new drug application. Typically, one study is sufficient to support a PMA application, as opposed to pharmaceutical approvals, which generally require two confirmatory clinical trials.

CONCLUSION

From a clinical trials perspective, the biggest changes in the device space are occurring in the 510(k) process. Domestically, the Center for Devices and Radiological Health has been requesting significantly more performance data. Future articles in this column will discuss some of the best strategies for success in the ever-changing regulatory landscape. ■

1. US Food and Drug Administration. Classify your medical device. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm. Accessed October 3, 2014.
2. US Food and Drug Administration. General and special controls. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/GeneralandSpecialControls/default.htm. Accessed October 3, 2014.
3. US Food and Drug Administration. Premarket notification (510k). http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketnotification510k/default.htm. Accessed October 3, 2014.
4. US Food and Drug Administration. Draft guidance for industry and Food and Drug Administration staff. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf. Accessed October 3, 2014

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