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Regulatory Update: Premarket Notification 510(k) Class II Devices

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The Premarket Notification (510(k)) pathway for medical device approval presents challenges for device manufacturers, FDA reviewers, and patients. The FDA has begun to modernize the 510(k) program to ensure the safety and efficacy of Class II devices. Class II medical devices present moderate risk to patients and require regulatory scrutiny beyond general controls. Forty-three percent of all cleared devices are Class II.[1] The original list of Class II devices was established in 1976, however the list has expanded over the last forty years through the approval of new Class II devices and the reclassification of Class I and Class III devices. For a product approved through the 510(k) pathway, a manufacturer must demonstrate the new device is (1) substantially equivalent to a Class II or 510(k) exempt device and, (2) as safe and effective as the predicate.[2]

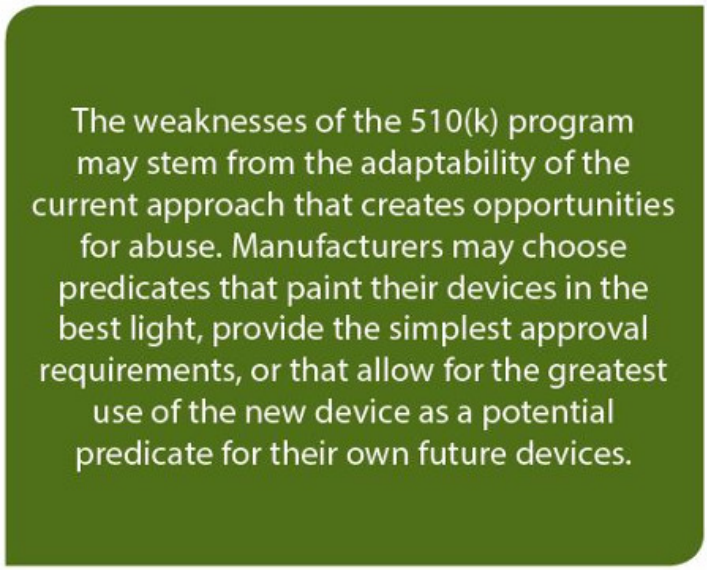
The weaknesses of the 510(k) program may stem from the adaptability of the current approach that creates opportunities for abuse. Manufacturers may choose predicates that paint their devices in the best light, provide the simplest approval requirements, or that allow for the greatest use of the new device as a potential predicate for their own future devices. Some manufacturers gravitate to older predicates because the performance testing conducted at the time of the original application is less strenuous than the testing conducted on newer devices. This permits manufacturers to seek clearance for new technology, with the potential to perform at much higher standards than existing predicates, by meeting the lower standards of legally marketed devices.

Predicate Creep or Generation Gap

Perpetual “predicate creep” compounds this situation.[3] By its very nature, a substantially equivalent device is similar but not identical to its predicate. However, if the new device is approved under a 510K, it becomes a potential predicate itself. After multiple submissions, new devices can be markedly different from the original predicate to which they are supposed to be substantially equivalent. Therefore, many new Class II devices are approved using performance criteria established by dissimilar predicate devices that are often several 510(k) generations removed. This problem has been particularly difficult for FDA reviewers to address because of the structure of the pathway. Once the FDA accepts a device as an appropriate predicate, direct comparison testing between the proposed device and the predicate is the established mechanism for review. However, FDA reviewers may be unofficially attempting to mitigate these dangers in non-structured and unexpected ways (by requesting additional product testing or human factors studies, for example), leading to frustration from device manufacturers. Patients are similarly frustrated by the existing 510(k) pathway because of the flexibility it allows manufacturers. A patient has no way to know if a new device is any better than one several generations old. Most consumers assume that all devices, since they have been reviewed and approved by the FDA, are equally effective. However, shortcomings in older technologies present the potential to undermine public trust in medical devices and the FDA.

Pathway to Modernization

In response to the problems, the FDA has implemented several new upgrades to the 510(k) regulatory pathway.[4,5] The agency’s efforts have been varied and impact many different aspects of the device approval and monitoring systems, including: pre-market requirements, the use of real world evidence in applications, substantial equivalency determinations, and post-market surveillance. Two particularly impactful changes are the newly established Safety and Performance Based Pathway, and the unofficially proposed 10-year cap on predicate devices.



The Safety and Performance Based Pathway (an expansion of the Abbreviated 510(k) pathway) has established a distinct means of putting a product on the market.[6] The purpose of the Safety and Performance Based Pathway is to allow certain devices to demonstrate they are as safe and effective as a predicate, despite technological differences, through means other than direct comparison testing. FDA will develop a list of device types that are appropriate for the pathway and develop guidance documents for each type.

Eligible devices must meet the following criteria: (1) have the same indications for use as the predicate, (2) not raise new questions of safety and effectiveness due to technological differences from the predicate, and (3) are one of the device types on the approved list. The device-type specific guidance documents outline the applicable performance criteria based on FDA-recognized consensus standards, special controls, and/or other guidance documents. FDA intends to periodically review and update the performance criteria as needed.

The purpose given by the FDA for the new pathway is to comply with the Least Burdensome provisions enacted in 2017,[7] which mandate that FDA require the minimum amount of information needed to make substantial equivalency determinations. The argument is that direct comparison testing is more burdensome for certain types of devices than meeting FDA's specified performance criteria. However, the pathway is likely also intended to address the problems surrounding lax testing requirements from old predicates. Given that the pathway is not yet operable, there is no way to know which direction the program will take. It may make 510(k) submissions cleaner and more straightforward or it may increase the requirements for certain device types. In either case, manufacturers will still have the option to submit a Traditional, Special, or Abbreviated 510(k).

Consequences of Retiring Decades-Old Predicates

The most radical proposed change to the 510(k) pathway surrounds the use of predicates more than 10 years old. FDA announced on November 26, 2018 in a statement8 from FDA Commissioner Scott Gottlieb that the Center for Devices and Radiological Health (CDRH) will consider publishing a list of devices cleared based on predicates more than 10 years old and retiring older devices as potential predicates. Currently, 20% of cleared devices use predicates older than 10 years.

The FDA puts forth the argument that newer devices include advanced technology far beyond older predicates. Consequently, direct comparison testing through decade old test methods fail to appreciate or account for issues of safety and efficacy raised by modern technology. The agency similarly argues that new technology should be held to the standard of other contemporary advancements. The proposed limit would be beneficial for patients, who could be assured that newly approved devices are as safe and work as well as their contemporary counterparts. The average patient likely already believes that a 2019 ultrasound is more trustworthy and advanced than one cleared in 1999. On the other hand, innovators would face an enormous burden. It would become more difficult to find a feasible or appropriate predicate with a much smaller pool of options.

Some devices that could have successful 510(k) applications with older predicates would need to find alternative regulatory pathways to market that could escalate the required pathway to a premarket approval (PMA) submission, or to a direct de novo request. Both of those alternatives are significantly more expensive and require much longer to complete. This reality makes the 10-year cut-off a double-edged sword. The high cost and length of an application may be prohibitive, particularly affecting devices in development, thus limiting access to newer technologies that could provide significant advantages to patients.

In Summary: Guidance to be Determined

The futures of the Safety and Performance Based Pathway and the 10-year limit on predicate devices are unclear. While there is a final guidance on the Safety and Performance Based Pathway, it is far from ready for implementation. The agency has not yet developed the list of eligible device types or drafted guidance documents to fulfill the pathway. The FDA will need to focus resources on building the list and developing the performance criteria for the guidance documents, and call for public comment and approval. The industry is years from a fully functional and usable pathway.

Changes in FDA Leadership

The future of the 10-year limit is even more tenuous. In January 2019, the agency officially requested public comment on the proposal to publish a list of cleared devices with 10+ old predicates.[9] The FDA did not specifically ask for comment on a ban on older predicates. With no proposed administrative regulation, guidance document, or statute to officially establish the 10-year limit, there is no way to know if FDA will follow through on this suggestion. However, there is a strong likelihood that the limit would be challenged under administrative law. Courts would need to consider a variety of compelling arguments to determine if FDA has exceeded its authority.

The resignation of Commissioner Gottlieb in March 2019[10] only compounds the outstanding questions. Will a new commissioner follow the path in progress to implement the changes, modify them to benefit either patients or industry, or abandon them entirely? The stakes are high for everyone involved and the public will be watching for signs of what is to come.

Development of new Safety and Performance pathway guidance documents and a revision of 510(k) guidance documents will be sure signs the agency intends to continue its modernization efforts. However, a newly nominated commissioner with industry background (or from the device world) may signpost an era where the strictest proposed 510(k) changes will fall by the wayside.

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