The U.S. Food and Drug Administration (FDA) released today its widely anticipated preliminary report/recommendation on revisions to the medical device 510(k) premarket clearance process. These changes will have a significant impact on medical device companies and the route they take to get devices to market. Below are some highlights and the official overview of FDA’s findings and recommendations. It is important to note that FDA has asked for public comments to the reports – a valuable opportunity to submit comments on this important issue.

**Highlights**

- Center of the overhaul is the 510(k) system that FDA uses to grant speedy approval to devices deemed similar to products already on the market. FDA critics say that high-risk devices, such as heart pacemakers, are increasingly slipping through the 510(k) process without thorough testing and scrutiny. Under the new regime, makers of medical devices would have to submit more safety information to win federal approval under a proposal designed to tighten regulation of thousands of products reviewed each year.

- Creation of a new class of devices that would require clinical evidence before gaining 510(k) approval. The designation would streamline the process for a small subset of devices by telling applicants up front what will be required to gain marketing clearance, thus avoiding delays. Currently, only 8 – 10% of the devices approved under the 510(k) moniker require clinical studies.

- Appointment of William Maisel as the device center’s chief scientist and a deputy director.

**Overview of Findings and Recommendations**

The aim of the 510(k) program is two-fold: (1) to assure, through a quality review process, that marketed devices, subject to general and applicable special controls, provide a reasonable assurance of safety and effectiveness; and (2) to foster innovation. Robust premarket review is an essential component of CDRH’s medical device oversight. CDRH’s postmarket tools, while valuable, have important limitations and are not sufficient to serve as a substitute for high-quality premarket review. At the same time, in order to facilitate innovation, the premarket clearance process must be reasonable and predictable.

An effective 510(k) program is predicated on three major elements. First, 510(k) decision making must be grounded in a rational, well-defined, and consistently interpreted review standard.

Second, the 510(k) program must support informed decision making by facilitating the collection of sufficient information to allow for well-informed, reliable decisions, and by providing an operational infrastructure and tools that enable FDA to make the best use of that information through knowledge development and knowledge sharing. Third, there must be appropriate systems and metrics in place to continuously assure quality, consistency, timeliness, and predictability, to the extent feasible, across the 510(k) program.

The 510(k) Working Group identified several areas for improvement related to each of these elements.

With regard to the 510(k) review standard, the Working Group found that key terms in the statutory definition of "substantial equivalence" have not been consistently interpreted by the center. In particular, there is insufficient clarity about what constitutes the same versus a new "intended use," and about when "different technological characteristics" raise "different questions of safety and effectiveness." Ambiguity at these critical decision points, at times, has contributed to inconsistency in CDRH’s 510(k) decision making. As the 510(k) standard has been applied to a wider range of devices over time, including increasingly varied, complex, and potentially higher-risk technologies, the need for greater clarity with respect to these terms has become even more pressing. The Working Group recommends that CDRH more clearly define these terms in guidance and training for review staff and industry.

Further, while the concept of "substantial equivalence to a predicate" is generally reasonable, CDRH’s application of this standard has, in certain cases, raised concerns. When a predicate has a well-established risk/benefit profile and is generally well-regarded by the healthcare community, a premarket comparison of a new device to that predicate, with sufficient information, can provide reasonable assurance that the device, subject to general and applicable special controls, is safe and effective for its intended use.

However, concerns have been raised that current FDA regulations and practice may allow for some types of predicate comparisons that are insufficient to consistently provide such assurance, including the use of predicates that have been withdrawn from the market due to issues of safety or effectiveness, and the use of so-called “split predicates,” a term that refers to using one predicate as the basis for a comparison with respect to "intended use" and another predicate as the basis for a comparison with respect to "technological characteristics." The use of a split predicate is akin to combining different attributes of more than one device into a single, nonexistent predicate device whose risks and benefits are unknown.

The Working Group recommends that CDRH consider taking steps, through guidance, to set forth factors regarding when a device should not be used as a predicate. Such factors should be well-reasoned, well-supported, and established with input from a range of stakeholders, and unintended consequences should be carefully considered. The Working Group also recommends that CDRH explore the possibility of explicitly disallowing the use of split predicates.

In addition to defining the 510(k) review standard more clearly, it is important for CDRH to use the tools it has to provide an appropriate,
risk-based level of regulatory control for devices that are determined not to have a valid predicate, but whose risks do not warrant a premarket approval approach. The process for Evaluation of Automatic Class III Designation, also known as the de novo classification process, is meant to serve as an alternative regulatory pathway for such devices; however, as currently implemented, it is inefficient and has not been optimally utilized across the center. The Working Group therefore recommends that CDRH take steps to streamline its implementation of the de novo process, and to assure that it is utilized appropriately across the center.

With regard to informed decision making, the Working Group found that it is challenging for review staff to obtain, in an efficient and predictable manner, sufficient device information to make well-supported decisions. To obtain such information without creating unnecessary delays and burden, CDRH must provide submitters with as much up-front clarity as feasible about its evidentiary expectations. The Working Group therefore recommends that CDRH take steps to foster the submission of high-quality 510(k) device information, in part by better clarifying its expectations for 510(k) content.

Most notably, the Working Group recommends that CDRH explore the possibility of developing guidance to define, as a heuristic, a subset of class II devices called "class llb" devices, for which clinical information, manufacturing information, or potentially, additional evaluation in the postmarket setting, would typically be necessary to support a substantial equivalence determination. Delineating between "class Ila" and "class llb" would not reconfigure the current, three-tiered device classification system established by statute; it would represent only an administrative distinction.

The development of a "class llb" guidance would provide greater clarity regarding what submitters would generally be expected to provide in their 510(k)s for certain types of devices. Although further deliberation would be needed to better characterize "class llb," potential candidates for this device subset may include implantable devices, life-sustaining devices, and life-supporting devices, which present greater risks than other class II device types.

The Working Group found that, in general, most instances where concerns were raised by industry and center staff about problems with the 510(k) program involved the small subset of devices for which staff requested clinical information, either to answer questions appropriate for a substantial equivalence determination, but sometimes in cases where the sponsor had no advance notice that such information would be needed, or to answer questions more appropriate for the de novo classification process.

Both scenarios have contributed to less predictability and longer time-to-decision in the 510(k) program. By creating a "class llb" device subset and making appropriate use of a streamlined de novo process, CDRH could make more predictable, timely, and consistent decisions.

The Working Group also found that limitations in CDRH's information technology and knowledge management infrastructure and tools make it difficult for center staff and external parties to readily access meaningful information that would help improve both the quality and the predictability of 510(k) decision making.

Because 510(k) decision making relies on a comparison to a predicate, review staff and submitters must have an adequate level of familiarity with predicate devices and past 510(k) decisions, supported by well-organized and easily accessible information, in order for the process to function properly. The Working Group therefore recommends that CDRH enhance its internal and public 510(k) databases to provide more complete, up-to-date device information to review staff and the center's external constituencies.

Finally, the Working Group found that there is a need for more robust systems and tools for quality assurance in the 510(k) program. Quality and consistency depend on a highly qualified, well-trained, and well-supported review staff, and on appropriate oversight. The Working Group therefore recommends that CDRH enhance its support for training and professional development for review staff. Further, currently there are insufficient tools and metrics in place to assess the consistency of decision making across the 510(k) program, and to track the program's public health impact quantitatively.

Although CDRH collects information on device performance in the postmarket setting, important limitations, including the inability to consistently link postmarket events to specific 510(k)s, make this information, in isolation, an unreliable measure of program effectiveness. The Working Group recommends that CDRH develop program metrics and better systems for continuous monitoring of 510(k) program performance and effectiveness, in part through the oversight of a new Center Science Council composed of experienced reviewers and managers, under the direction of the Deputy Center Director for Science.

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