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FDA'S 510(K) WORKING GROUP RELEASES PRELIMINARY REPORT AND RECOMMENDATIONS

On August 4, 2010, FDA's Center for Devices and Radiological Health (CDRH) released its 510(k) Working Group Preliminary Report and Recommendations. The Working Group Report outlined the group's findings regarding observed deficiencies in 510(k) process and set forth preliminary recommendations for improving the process.

Although the Working Group recommended that the current regulatory scheme be left largely intact, many of the proposed recommendations could have significant implications for the future development and clearance of devices through the 510(k) pathway. Some of the more significant recommendations include (i) further defining key terms used to determine "substantial equivalence"; (ii) establishing a new subclass of medical devices (denoted as "Class IIb") that generally require a greater amount of data and information for 510(k) clearance, including clinical data; (iii) seeking authority for the agency to evaluate potential off-label uses of a device when considering clearance of a device; (iv) limiting the use of more than one predicate in a 510(k) notification and potentially disallowing "split predicates"; (v) modifying the de novo classification process to encourage greater use of that process; (vi) revising the circumstances under which device modifications require a new 510(k) submission; and (vii) establishing a process to rescind 510(k) clearances.[1] Some of these recommendations can be implemented by FDA immediately, while others would require statutory changes.

This alert provides background on the 510(k) notification process, an overview of some of the more significant aspects of the Working Group's Report, and initial observations regarding potential implications of the Report on the future development of medical devices.

I. BACKGROUND

The premarket notification process, commonly referred to as the "510(k)" process, is a regulatory pathway for new medical devices to enter the market. Under this process, before introducing a new medical device to the market, the sponsor must provide a notification to FDA that demonstrates that the new device is "substantially equivalent" to a device already legally on the market that does not require a premarket approval application (PMA). Class III, high-risk devices generally require a PMA, meaning that the 510(k) process is typically used for class II, moderate-risk devices and class I, low-risk devices that have not been exempted from premarket notification by statute or regulation.

The primary issue for review in this process is whether the device is substantially equivalent to a legally marketed predicate device.[2] Under the current statutory definition of the term, a device is

[1] CDRH also released a report by the Task Force on the Utilization of Science in Regulatory Decision Making regarding methods to respond to evolving information about products, novel technologies with which FDA has no experience, and new scientific methods to help analyze data.

[2] *See* Center for Devices and Radiological Health, 510(k) Working Group Preliminary Report and Recommendations 24-33 (2010) (hereinafter "Report").

regarded as substantially equivalent if it has the same "intended use" as a predicate, and it "has the same technological characteristics as the predicate device" or has different technological characteristics, but the new technology "does not raise different questions of safety and effectiveness than the predicate device."[3]

In addition to this process, new devices for which there is no substantially equivalent predicate may be cleared for entry into the U.S. market through what is commonly referred to as the de novo classification process. For devices that are low or moderate risk but lack an appropriate predicate, the sponsor may -- following a determination that the device is not substantially equivalent to a predicate -- request de novo classification as a class I or II device.[4] De novo classification is frequently a lengthy process requiring the development of clinical data to support the regulatory classification. For this reason, relatively few devices enter the market through the de novo pathway.

Since its establishment, the 510(k) notification process has been an important pathway for devices to enter the market, striking a balance between the flexibility needed to foster innovation and the appropriate level of regulatory oversight. In the years 2003 through 2007, for example, CDRH reviewed over 13,000 510(k)s and cleared approximately 90% of the submissions, compared to approximately 1,000 PMAs and PMA supplements.[5]

The 510(k) regulatory scheme, however, has not been without criticism. Some groups have claimed that the 510(k) process does not have sufficient controls to ensure that new devices are appropriately safe and effective. Because the 510(k) process is an iterative process that allows sponsors to claim substantial equivalence to any predicate, many have claimed that "technology creep" has allowed unproven devices to enter the market. In turn, others have claimed that FDA's application of the 510(k) process has been inconsistent and unpredictable, with the agency increasingly imposing cumbersome data requirements without justification. Echoing some of these criticisms, in 2009, the Government Accountability Office issued a report concluding that the system contains weaknesses and needed to be improved.[6]

In light of these criticisms, FDA announced that it would conduct a comprehensive assessment of the 510(k) process. To this end, the agency asked the Institute of Medicine (IOM) to perform a study that is expected to be completed by next summer. At the same time, in September 2009, CDRH convened an internal group of CDRH officials to conduct an internal review of the 510(k) process. As described in the Report, the Working Group gathered input from CDRH employees and managers and a range of external constituencies on how the 510(k) process currently operates, what challenges it presents for CDRH staff and others, and what steps the Center might take to improve the program. The Working Group also collected and analyzed relevant data from CDRH's internal databases to identify trends in the review of various types of 510(k) submissions. The "preliminary report" is intended as a first step in potential reforms to the 510(k) process.

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[3] Federal Food, Drug, and Cosmetic Act (FDCA) § 513(i)(1)(A), 21 U.S.C. § 360c(i)(1)(A).
[4] FDCA § 513(f)(2), 21 U.S.C. 360c(f)(2). In addition to traditional and de novo 510(k)s, FDA has also developed other types of 510(k)s intended to be less time-consuming than traditional 510(k)s. These include Special 510(k)s and Abbreviated 510(k)s that are generally used to clear modified devices without fundamental changes to technology and devices for which consensus standards exist.
[5] GAO, Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved Through the Most Stringent Premarket Review Process (2009), *available at* http://www.gao.gov/products/GAO-09-190.
[6] *Id.*

II. SIGNIFICANT OBSERVATIONS AND RECOMMENDATIONS INCLUDED IN THE WORKING GROUP REPORT

New Class IIb

A diverse set of devices is currently subject to the 510(k) requirement -- both in terms of technological complexity and potential risk to patients. While lower risk or technologically simple devices may be cleared without the need for new clinical data, complex or higher risk devices typically need more robust 510(k) submissions. According to the Working Group Report, however, the agency often receives submissions lacking the information required to make a substantial equivalence determination. The Report observed that "[i]t is challenging for CDRH to obtain, in an efficient and predictable manner, the information it needs to make well-supported premarket decisions and assure that each new or modified 510(k) device is substantially equivalent to a valid predicate."[7] Accordingly, the Report recommended the development of a class II subset called "class IIb." The goal of creating this subset would be to identify groups of devices for which more extensive data are typically needed.

The Report indicated that clearance of devices in the class IIb subset would usually require the submission of clinical information and manufacturing information, and in some cases the use of post-market evaluation. With respect to clinical data, the Report noted that 510(k)s are increasingly used to clear complex devices for which the safety of a modification to a device can be measured only by clinical investigation. It recommended that the creation of a class IIb subset be used as a vehicle to offer a clearer picture when clinical data will be needed and what form it should take. On the issue of post-market surveillance, the Report noted that "it might not be feasible" to conduct a large-scale clinical trial of a device containing novel and complex technologies, and therefore it may be necessary to collect additional data over a longer period of time to better assess safety and effectiveness. Nevertheless, the Report noted that the FDCA does not provide explicit authority to require post-market studies for most 510(k)-cleared devices.[8]

The agency suggested that, if implemented, this recommendation "would not reconfigure the current, three-tiered device classification system established by statute." Rather, delineating between Class IIa and Class IIb "would represent only an administrative distinction."[9]

Clarifying Substantial Equivalence

The Working Group also observed ambiguities regarding key terms that are involved in the substantial equivalence determination. Specifically, the group identified confusion regarding "intended use" versus "indication for use," which CDRH has used interchangeably in some documents. The Report also observed difficulties applying the "different technological characteristics" and "different questions of safety and effectiveness" standards. The Report recommended that CDRH provide guidance to clarify these terms.

Evaluating Off-Label Uses

The Working Group Report concluded that another issue with the 510(k) process is the possibility that devices sometimes obtain 510(k) clearance for an intended use that does not match the device's actual use in practice. The substantial equivalence standard requires the device under review to have the "same intended use" as the predicate device, but according to section

[7] Report, *supra* note 2, at 10.
[8] *Id.* at 78.
[9] *Id.* at 5.

513(i)(1)(E) of the FDCA, "any determination by [FDA] of the intended use of the device shall be based upon the proposed labeling submitted in a report for the device under section 510(k)." The Report observed that, in some cases, the "true" intended use of the product could raise different questions of safety and effectiveness.[10] Given that the statute limits FDA from looking beyond the labeling to establish intended use, the Report recommended that CDRH "explore the possibility pursuing a statutory amendment to section 513(i)(E) of the FDCA."[11]

Disallowing Split Predicates

The Working Group observed that "CDRH's current practice allows for the use of some types of predicates that may not be appropriate."[12] In particular, the Working Group took issue with the practice of "split predicates" -- a situation in which the sponsor claims substantial equivalence to the intended use of one predicate and the technological characteristics of another. According to the Report, "this practice is akin to combining different attributes of two or more devices into a single, nonexistent predicate device that may bear little resemblance to the device under review or to any marketed device."[13] This practice is different from the concept of multiple predicates, a situation in which a device claims substantial equivalence to several distinct predicate devices. The Report noted that some 510(k) submissions include up to five or more predicates.

According to the Working Group Report, a survey of CDRH staff revealed a division in opinion regarding the acceptability of using split predicates. The Report recommended that CDRH develop guidance on the use of more than one predicate and clarify the difference between split and multiple predicates. It also recommended that CDRH consider explicitly disallowing the use of split predicates.

Enhancement of the De Novo Review Process

The Working Group Report observed that the de novo review process, as currently implemented, is inefficient and has not been utilized optimally across the center. The group recommended that CDRH encourage pre-submission engagement between submitters and review staff to discuss the appropriate information to provide to CDRH for devices eligible for de novo classification, in lieu of the exhaustive 510(k) review that currently precedes de novo classification. The Report also recommended that CDRH consider establishing a generic set of controls that could serve as baseline special controls for devices classified into class II through the de novo process.

Modification Guidance

The working group also recommended that CDRH explore revising existing guidelines for when changes to a device require a new 510(k) or can be handled through other regulatory mechanisms, such as a letter to file or a Special 510(k). The Report notes that submissions sometimes reference as predicates devices whose modifications the agency never reviewed, in some cases requiring CDRH to assess the safety and efficacy of both the modified predicate device and the device seeking 510(k) clearance. The Report also suggests that CDRH explore "the feasibility of requiring each manufacturer to provide regular, periodic updates . . . listing modifications made to its device without the submission of a new 510(k), and clearly explaining why each modification noted did not require a new 510(k)."

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[10] *Id.* at 50.
[11] *Id.* at 51. Presumably, the Report means to reference section 513(i)(1)(E).
[12] *Id.* at 8.
[13] *Id.* at 59.

Rescission Authority

The Report recommends that CDRH consider issuing a regulation defining the grounds and procedures for rescinding a 510(k) clearance. The report states that such authority is "inherent" in the agency's discretion to reconsider its decisions, and it references FDA's 2001 proposed rule on the rescission of substantial equivalence decisions. The report does not discuss how the agency should handle the practical consequences of a rescission process -- for instance, the effect of a rescission on already-cleared 510(k)s that reference the rescinded device as a predicate.

Other Recommendations

Some other notable recommendations included:

- CDRH's decisions regarding the criteria for when a device may be considered a predicate are inconsistent and have led to inappropriate 510(k) clearances. CDRH should develop guidance to explain when a device will be disqualified as a predicate due to safety or efficacy concerns.
- CDRH should enhance its support for training and professional development for review staff.
- CDRH should improve the tools and metrics used to assess the consistency of decision making across the 510(k) program, and should track the program's public health impact quantitatively.
- CDRH should clarify the circumstances under which it will refuse to clear a device due to manufacturing concerns.
- CDRH should develop a public, easily searchable database that contains 510(k) summaries, photographs, schematics, and explanations of how 510(k)s relate to one another.

III. OBSERVATIONS AND NEXT STEPS

The recommendations of the 510(k) Working Group are far reaching and have the potential to significantly impact the development and clearance of devices under the 510(k) pathway. Some of the recommendations have the potential to provide useful improvements to aspects of the 510(k) process. For example, streamlining the de novo 510(k) process and bringing additional clarity to the standards and definitions used by FDA have the potential to provide greater predictability to the 510(k) process. Similarly, developing a public, easily searchable database that contains more information about cleared 510(k)s could provide greater transparency and a better source of information about predicates.

Other recommendations, however, could impose new regulatory barriers that unnecessarily limit the utility of the 510(k) pathway. For example, limiting the use of multiple or split predicates could impose unnecessary burdens. Requiring devices that combine well-established intended uses and known technological characteristics to proceed down the PMA or de novo pathway simply because there is not a single predicate combining these elements could limit the utility of the 510(k) pathway. Similarly, while clarifying the standards used by FDA has the potential to improve the 510(k) process, if FDA's guidance is unnecessarily restrictive, it could further inhibit investment and innovation.

Moreover, aspects of the Working Group Report raise questions about the extent to which FDA could implement the recommendations without new statutory authority. For example, the Working Group's recommendation to create a new Class IIb subset raises a question regarding the agency's authority to manipulate the current regulatory scheme without seeking Congressional intervention. On one hand, the FDCA clearly lays out three device classifications, and it arguably does not leave room for the agency to alter that scheme further. On the other hand, the class IIa/IIb division could be viewed simply as a way of ordering the types of information it expects to see in a 510(k) submission. A

similar question arises with respect to the agency's authority to rescind a 510(k) device. Other recommendations, such as the ability of the agency to consider off-label uses of a device when considering a 510(k), clearly require statutory changes.

FDA has established a public docket regarding the Working Group Report that will be open for public comments until October 4, 2010.[14] If you have questions about the 510(k) process or the Working Group Report, or would be interested in submitting comments to FDA, please feel free to contact any of the attorneys listed below.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our food & drug practice group:

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[14] 75 Fed. Reg. 47307 (Aug. 5, 2010).