



February 4, 2010

**FDA Announces Public Meeting Regarding
510(k) Review Process**
King & Spalding to Submit Oral and Written Comments

For more information, contact:

Edward M. Basile
(202) 626-2903
ebasile@kslaw.com

Laurie A. Clarke
(202) 626-2645
lclarke@kslaw.com

Lynette A. Zentgraft
(202) 626-2996
lzentgraft@kslaw.com

Elaine H. Tseng
(415) 318-1240
etseng@kslaw.com

Jessica M. Ringel
(202) 626-9259
jringel@kslaw.com

**King & Spalding
Washington, D.C.**
1700 Pennsylvania Avenue, NW
Washington, D.C. 20006-4707
Tel: (202) 737-0500
Fax: (202) 626-3737

San Francisco, CA
101 Second Street
Suite 2300
San Francisco, CA 94105
Tel: (415) 318-1200
Fax: (415) 318-1300

www.kslaw.com

On January 27, 2010, the Food and Drug Administration (FDA or the Agency) announced in the *Federal Register*, 75 Fed. Reg. 4402, a public meeting entitled “Strengthening the Center for Devices and Radiological Health’s 510(k) Review Process.” FDA described the purpose of the meeting as: “to identify actions that the Center for Devices and Radiological Health (CDRH) can consider taking to strengthen the premarket notification process for review of medical devices, also known as the 510(k) process.” The meeting will take place from 8:00 a.m. until 5:30 p.m. on Thursday, February 18, 2010 at the Hilton Washington DC North in Gaithersburg, MD. Attendees must register online by February 12, 2010 at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/default.htm> and indicate if they want to make a presentation. A live webcast will be available at: <http://www.ConnectLive.com/events/fda021810>.

In September 2009, FDA requested the Institute of Medicine (IOM) to conduct a comprehensive study of the 510(k) process. Because the results of the IOM study are not expected until March 2011, FDA convened an internal working group to recommend actions that CDRH could take in both the long and short term to strengthen the 510(k) program. The February 18 public meeting is a result of the working group’s efforts. The meeting will focus on four areas of FDA concern: predicate devices, new technologies and scientific evidence, practices CDRH has adopted in response to the high volume of 510(k) submissions, and postmarket surveillance and new information about marketed drugs.

The meeting will include presentations from FDA and the public and a round-table discussion. In the *Federal Register* notice, FDA lists detailed questions related to the four discussion topics. The questions reveal some concerns FDA has regarding the 510(k) process; the issues and questions are summarized below. Written comment on these topics may be submitted until March 5, 2010.



FDA & Life Sciences Practice Group

King & Spalding has registered to present oral comments at the public meeting. We also plan to submit written comments to FDA. We welcome your input regarding FDA's questions.

Issues Related to Predicate Devices

The first set of questions relate to the 510(k) database on CDRH's website, which contains copies of cleared devices' substantially equivalent letters, the indications for use, and the 510(k) summary. FDA seeks comments on how effective and useful the database is for entities seeking to evaluate the adequacy of potential predicate devices and to write substantial equivalency explanations for their own 510(k) submissions. The Agency is interested in what aspects of the database are useful and which could be improved, how effectively the database describes cleared devices, and what improvements could be made. Notably, FDA questions whether it should "require 510(k) holders who receive a substantial equivalence decision for their device to submit a redacted version of their 510(k) submission after clearance, for public release."

Second, FDA expresses concern that "[s]ome 510(k) submitters do not accurately portray the similarities and differences between the device under review and the predicate device(s)." The Agency seeks input about whether these inaccuracies are due to a lack of sufficient information about potential predicate devices, or whether there are other contributing factors.

A third area of concern related to predicate devices is the current eligibility of 510(k) devices to serve as predicate devices when the device is no longer in use, is not "relevant to current standards of care," or has been made obsolete by newer technology. FDA would like commenters to discuss the impacts of this policy and whether the criteria for eligibility to serve as a predicate device should be stricter.

FDA's fourth set of questions are related to "predicate creep" and "non-inferiority creep." FDA defines predicate creep as "[i]ncremental device changes [that] may seem innocuous individually" but that combine over successive 510(k) submissions "to create a device that is significantly different from the original device." The Agency defines non-inferiority creep as the outcome of successive non-inferiority studies submitted as evidence of substantial equivalence, so that "device B is non-inferior to A, device C is non-inferior to B, and device D is non-inferior to C." In this case, the outcome may be that the "difference in effectiveness between device A and D may approach clinical significance." FDA is seeking advice on any changes in the 510(k) process that could combat predicate and non-inferiority creep, and whether there are any "circumstances under which FDA should consider a more thorough review of multiple incremental device changes between 510(k) submissions, or a more thorough review of the appropriateness of clinical non-inferiority studies when assessing differences in device safety and effectiveness."

Fifth, FDA seeks input regarding "split predicates," in which one or more predicate devices are used to establish substantial equivalence (*e.g.*, one device is used for intended use, and another for the technological characteristics). FDA is concerned that a 510(k)-cleared device that uses a split predicate "may be very different from any other device on the market." FDA's only question on this topic is "whether the use of a split predicate or more than one predicate serves the public health goals of the 510(k) program," perhaps signaling the Agency's unease with the practice.



FDA & Life Sciences Practice Group

Finally, FDA asks a series of questions related to the flowchart that the Agency uses to determine whether a device has the same intended use as the predicate device (available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM081395.pdf>.)

Currently, the flowchart distinguishes between “indication for use” and “intended use,” and allows for a different indication for use between the predicate and the substantially equivalent device, as long as the intended use is the same. FDA seeks comments concerning the meaning of these terms, whether the use of two terms is appropriate, and what advantages and disadvantages the use of the two terms creates.

Issues Related to New Technologies and Scientific Evidence

FDA’s second set of questions pertain to new technology and scientific evidence. First, FDA asks for suggestions on what features should be considered to be “different technological characteristics” (defined by the FDCA to mean “a significant change in the materials, design, energy source, *or other features* of the device from those of the predicate device.” FDCA § 513(i), 21 U.S.C. § 360c(i) (emphasis added)). FDA seeks comments on what should and should not be “other features” that FDA considers to be different technological characteristics.

Second, FDA seeks advice on what criteria it should use to “determine which risks can be mitigated through general controls alone or with special controls, and which risks are sufficient to make the device ineligible for *de novo* review of automatic Class III classification” for devices that are found to be Not Substantially Equivalent to a predicate device and are subsequently classified as Class I or Class II devices.

FDA’s third set of questions in this category concerns the current practice under which a device with technological characteristics that are different from those of the predicate device may still be considered substantially equivalent. This can happen if the applicant submits information “that demonstrates that the device [under review] is as safe and effective as a legally marketed device” and that the device under review “does not raise different questions of safety and effectiveness than the predicate device.” FDA seeks input regarding how to identify and characterize the pertinent risks associated with new technologies, whether there are any types of new technologies that are inappropriate for clearance through the 510(k) process, and how to define “different questions of safety and effectiveness.”

Fourth, FDA notes that in some situations, it may consider evidence from comparison studies to determine substantial equivalence. These types of studies are: “(1) [a] comparison of specifications to an FDA-recognized standard; (2) a comparison of specifications through bench testing; (3) a comparison of specifications through bench and animal or bench and clinical testing; or (4) a comparison of specifications through bench, animal, and clinical testing.” FDA requests commenters to describe situations under which each type of comparison study may be appropriately used. FDA also questions whether there are “circumstances under which one could show that a device is at least as safe and effective as the predicate” without conducting a large non-inferiority study. The Agency further queries the circumstances under which comparative studies of types (2), (3), and (4) are appropriate.

FDA next asks whether it has provided “sufficiently clear guidelines” regarding the provision of engineering and design information for devices under 510(k) review. The Agency is concerned because some 510(k)



FDA & Life Sciences Practice Group

submissions do not provide enough information “to enable FDA to have a sufficient understanding of how the device operates, and whether there are any design issues that would prevent it from operating as intended.”

Sixth, FDA queries whether it would be “beneficial” for FDA to be able to withhold an initial classification decision based on a manufacturer’s failure to comply with current good manufacturing (cGMP) requirements or other provisions of the FDCA that are not directly related to a substantial equivalence determination.

FDA also seeks input on whether new 510(k) devices should be required to have an indication for use that is “proven to FDA to provide clinical utility” (e.g., use in treatment or diagnosis of a specific condition). Currently, some submissions contain indications for use that are not associated with specific clinical utilities and FDA seeks examples of such devices and whether the lack of information about their clinical utility in their indications for use statements is “beneficial, harmful, or neither.”

Finally, FDA asks for comments regarding the effectiveness of the procedures used to curb off-label uses that could cause harm (as described in “Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff (Update to K98-1),” available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082162htm>, and whether and how FDA should modify its current approach.

Issues Related to Practices CDRH has Adopted in Response to a High Volume of 510(k) Submissions

The third set of questions about which FDA seeks comments is related to the large number of 510(k) submissions that the Agency receives every year. CDRH currently uses “a number of practices to allow for less resource-intensive reviews, including the third party review program, the Special 510(k) under the 510(k) Paradigm, bundling of devices in 510(k) submissions, and reliance on 510(k) submitters’ assertions of conformance to recognized standards (as in the Abbreviated 510(k) program).” Additionally, CDRH frequently relies on a single reviewer to review a submission. FDA seeks “comment on the advantages and disadvantages of each of these practices,” as they affect “the quality and timeliness of 510(k) reviews.”

Issues Related to Postmarket Surveillance and New Information about Marketed Devices

Finally, FDA asks some questions regarding postmarket surveillance and postmarket information about 510(k)-cleared devices. First, FDA asks whether it would be beneficial to impose a requirement to conduct postmarket surveillance studies on 510(k)-cleared devices.

Second, the Agency seeks input whether it should have the ability to rescind 510(k) clearance under a broad range of circumstances, and, if so, what criteria should be used to support a rescission.

Third, FDA asks whether and how postmarket information regarding 510(k)-cleared devices (e.g., adverse event reports, recalls, inspectional findings) should be used in the decision whether to grant 510(k) clearance to *similar* devices.



FDA & Life Sciences Practice Group

FDA next asks whether it would be beneficial for FDA to review and approve the labeling of some or all 510(k) devices after the devices have been cleared, but before initial marketing has begun.

Finally, FDA seeks input whether and how it should exercise more authority in situations in which a 510(k) has been purchased, sold, or transferred, but FDA has not been notified of the purchase, sale, or transfer.

* * *

Please contact us if you want to discuss FDA's questions, obtain our assistance in preparing your company or organization's oral and/or written comments, or share your views on these issues with us.

Celebrating 125 years of service, King & Spalding is an international law firm with more than 800 lawyers in Abu Dhabi, Atlanta, Austin, Charlotte, Dubai, Frankfurt, Houston, London, New York, Paris, Riyadh (affiliated office), San Francisco, Silicon Valley and Washington, D.C. The firm represents half of the Fortune 100 and, according to a Corporate Counsel survey in August 2009, ranks fifth in its total number of representations of those companies. For additional information, visit www.kslaw.com.

This alert provides a general summary of recent legal developments. It is not intended to be and should not be relied upon as legal advice.