

## CLIENT ALERT October 2009

### **Dr. Donna Bea Tillman, Director of the Office of Device Evaluation, Highlights Changes Coming in the 510(k) Program.**

On October 9, 2009, I moderated a panel on the 510(k) program at the Orthopedic Surgical Manufacturers Association (OSMA). OSMA has a very knowledgeable membership in the orthopedic and spine sectors. The 510(k) panel that I moderated was populated by Laurie Clarke from King & Spalding; Marie Marlow, President of M Squared, Inc., a regulatory consulting firm; and Elana Leventhal a legislative staffer for Congressman Pallone of New Jersey. You may or may not know that Congressman Pallone was one of the four members of the New Jersey delegation that assisted ReGen with the FDA and today the company is being criticized for it. And Congressman Pallone along with Congressman Waxman has held hearings on the future of the 510(k) program and more are planned for the future. The panel was interesting and informative—we shared thoughts about the state of the 510(k) program and the difficulties in obtaining a 510(k) today. We also attempted to convey opinions to and solicit thoughts from Ms. Leventhal about the importance of the 510(k) program to industry. Many attempted to convey that what is wrong with the 510(k) program stems from FDA's implementation of it today and not that the statute needs to be changed. The audience did not want Congress to tinker with the 510(k) program.

The most interesting insights preceded our panel. Speaking before our panel was Dr. Donna Bea Tillman, Director of the Office of Device Evaluation (ODE); Mark Melkerson, Director of the Division of Surgical, Orthopaedic, and Restorative Devices; and Jonette Foy, Branch Chief (OJDB). By far the most provocative and interesting comments came from Dr. Tillman. She was a last minute addition to the meeting by her own request. She said she was trying to make the rounds with meetings like this to get the word out about the things they are working on with the 510(k) program. Allotted thirty minutes, she packed in a lot of information. Her slides should soon be publicly available on FDA's website. If any of you would like them sooner please let Abbey Feldkamp know at [feldkamp@duvalfdalaw.com](mailto:feldkamp@duvalfdalaw.com) and we can send them to you. We encourage you to read them.

Dr. Tillman highlighted changes in the Agency's position on 1) posting 510(k) memos, 2) the definition of least burdensome and 3) clearance standards. She also discussed setting up a working group to address these issues through guidance documents. The following is a summary with my comments.

- 1) **POSTING 510(k) MEMOS.** Dr. Tillman noted CDRH will begin posting 510(k) memos by the end of the year which will help the public understand the rationale for new clearances. She said OIVD has already been posting these memos. This is meant as a way to make the Agency's thinking on clearances more transparent.

**COMMENT:** This is a great development and will be useful in understanding FDA's current thinking when planning for submissions. It also could provide unwanted guidance to competitors seeking subsequent clearances by providing more of a roadmap.

- 2) **(RE)DEFINING LEAST BURDENSOME?** Dr. Tillman stated the term "least burdensome" means "appropriately burdensome" and sponsors should understand that the Agency will want adequate data submitted in support of a 510(k) submission. The FDA thinks sponsors believe that least burdensome means barebones substantiation and initial submissions are often geared that way. Sponsors should not be surprised when the Agency asks for more. She added that as science improves and the FDA knows more, FDA may not limit its inquiry to questions asked in the past. They may want more substantiation than was provided in the past for predicate devices.

**COMMENT:** The concern industry has is "when will the FDA get its review staff's seemingly insatiable appetite for more information under control and within the realm of reasonableness?" Least burdensome means just that—"least" burdensome, not "appropriately" burdensome. We tried to ascertain how she could take that position. She probably derived this conclusion from a least burdensome (LB) guidance document that the Agency created (the word "appropriate" is not found in the statute or regulations) which defines LB as "a successful means of addressing a premarket issue that involves the *most appropriate* investment of *time, effort, and resources* on the part of FDA and industry." See "The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles; Final Guidance for FDA and Industry" at page 2. We might be even agreeing with Dr. Tillman if the word "appropriate" was put into proper context. The dual goals of the Agency that LB are designed to help are a) to *expedite availability* of new device technologies, and b) *without compromising* the scientific integrity in the decision-making process or FDA's ability to protect the public health. Admittedly today, FDA emphasis is overwhelmingly on protecting the public health to the detriment of failing to approve in a timely way important new therapies. We have not seen such conservatism and propensity for risk aversion in our entire careers doing FDA work.

\* **Using "Smart Science."** Evidence requested by FDA could be very well appropriate, but not necessarily the least needed to reasonably prove the scientific point at hand. FDA's LB guidance tells us that *smart science means acknowledging what is known and prove only what is unknown*. LB principles require only allow FDA to request the amount of information needed to answer the unanswered questions of safety and effectiveness.

\* **An Imbalanced Risk/Benefit Equation.** FDA reviewers often use these undefined terms to their advantage. They often extract more information than they are entitled to request and it is difficult to argue otherwise. We, as an industry, are totally dependent upon their self-imposed professionalism, strict adherence to the law, ethics and sense of scientific balance. But when they are taught to protect at all cost, the system becomes skewed and often demands far more evidence than is needed to clear or approve products. The whole clearance/approval process is a risk-based system and if we elevate the goal of "protection" to such a high level, patients will be deprived of the benefits of devices.

FDA staffers know that they have the upper hand because appeals are time consuming and expensive. If FDA's review staff is allowed to completely circumvent the statutory 510(k) requirements under the banner of protecting the public, then no request is unnecessary or irrational. If protection of the public were pursued to its logical end there would be three outcomes: a) little to no risk taken by the Agency in 510(k) clearances, b) the risk would not be balanced with the other half of FDA's mission—speeding innovations that help patients to market, and c) least burdensome principles would be a hollow and unenforced concept. FDA's review staff is required to rely on precedence—what is institutionally known by the agency about **predicates** and **other non-predicate but related**

**products**, as well as **similar technologies, materials, testing, etc., which FDA has seen in unrelated products**. This institutional knowledge is powerful and should inform FDA's decisions and reduce its informational requests to industry in making 510(k) clearances.

- 3) **STANDARD FOR CLEARANCE**. With respect to the standard for approval, Dr. Tillman broke it down into a discussion of what to do with 1) new indications, 2) new technological characteristics, and 3) the level of evidence necessary to clear devices. Dr. Tillman said they were going to try to develop guidance documents on each of these and publish them by year end and implement them by spring.

**New Indications**. On the topic of new indications, Dr. Tillman recently wrote an internal memo to CDRH review staff which was leaked to the press. In the memo she asks that all requests for new indications in 510(k) submissions be sent to her office, not necessarily for action, but so she can track the requests for new indications. In her slides at the OSMA she asked the following questions:

- 1) "How can we more clearly delineate the distinction between the 'indications' and 'intended use'?"
- 2) When does a new indication become a new intended use?;
- 3) How should substantial equivalence be interpreted when comparing two devices with different indications?; and
- 4) "How should we look at labeling?"

**COMMENT:** Starting with these questions Dr. Tillman has directed ODE staff to develop a policy to determine when a sponsor's new indication for use is actually a new intended use [Note: We thought that was the purpose for the "General vs. Specific Use" Guidance Document—indirectly]. If and when FDA concludes a new indication is a new intended use, the Agency can issue a Not Substantially Equivalent (NSE) letter. Her thinking is that too many devices are being cleared for uses not contemplated in the original clearance and FDA has to have some mechanism for dealing with these new uses which may require a PMA (or a de novo).

If FDA uses this construct to allow them to issue NSE letters, then sponsors would be automatically classified as a Class III device. Our concern is that it would be fairly easy for FDA to conclude that a new indication amounts to a new intended use for any product. If they reach that conclusion the product could be automatically classified into a Class III device requiring a PMA. There are times when a new indication is clearly a new intended use and there are times in which a new indication is clearly within an intended use, but different enough that the Agency may need more data to substantiate its safety and effectiveness. The solution in the latter case (same intended use, new indication) is not for FDA to give the sponsor a NSE letter and allow the device to be automatically classified into Class III. Instead, FDA could ask for more data under the 510(k) or allow for a de novo submission and clearance.

\***Same Technological characteristics**. Dr. Tillman then commented upon the second requirement in a 510(k)—that there be the same technological characteristics. She questioned when does a new question raise a "new type" of question? She was not clear where she was going with this point, but asked the following questions:

- 1) "When is a new question a 'new type' of question?;
- 2) How 'new' does the question need to be?;
- 3) What is the best role for standards?; and

- 4) When do device modifications trigger the need for a new 510(k)? (Current guidance targeted for update this year).”

**COMMENT:** Again, by parsing this out and dwelling on this criterion, the Agency may find another convenient avenue for issuing a NSE letter. If, FDA’s argument would be, the new technological features raise new types of questions, as opposed to simply new questions of a similar type, the FDA could find a product NSE without going further. New questions of a similar type are those in which the question may be new to the sponsor’s device because one of the device’s features is new and unlike that found in the predicate. But if the technology in question has been encountered before by the Agency, albeit in another device in the same or different therapeutic segment, the FDA can and should draw upon its institutional knowledge in assessing the sponsor’s 510(k) application. The FDA should not rigidly compartmentalize its knowledge base to knowledge only known in reviewing devices of a similar type. It can and should consider its knowledge as a whole.

**\*Level of Evidence Necessary.** The last issue of the three raised is the level of evidence necessary. Dr. Tillman emphasized that times have changed and she asked “how good is good enough?” She postulated what does FDA do when science changes, stick their heads in the sand and ignore it just to ensure consistency in clearances? She said consistency is important, but they must account for changes in science. She also asked how the Agency should factor in post-marketing information. She also wondered how clinical data will fit into future 510(k) s and what is the appropriate role for advisory panels?

**COMMENT:** The problem with this analysis/approach is it provides a built-in excuse to allow FDA to always ask for more in the name of science (and ergo, safety). Since when has science not always improved our existing knowledge? What this analytical bias ignores is the other side of the equation, i.e. that the 510(k) path also allows us to benefit from what is already known. Certain characteristics (e.g., biocompatible materials) in products and approaches (e.g. catheters, balloons) with products are deemed safe and effective because they’ve been in use and have demonstrated it. The 510(k) process can and should consider what is known.

- 4) **WORKING GROUP ESTABLISHED.** Dr. Tillman had much more to say that day about referring the 510(k) program to the Institute of Medicine (IOM) for an independent review and other comments. Importantly, she did state that CDRH has established a working group to look at these questions. They will consider past practices—what is working and what is not. They will be soliciting input from stakeholders before taking any significant action. We need to get involved as an industry.