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**CALIFORNIA HEALTHCARE  
INSTITUTE**

# **UPCOMING CHANGES TO THE 510(K) PROCESS**

**NEW APPROVAL PATHWAYS  
AND THE IMPACT ON  
MEDICAL DEVICE  
DEVELOPMENT AND  
INNOVATION**



# **Upcoming Changes to the 510(k) Process: New Approval Pathways and the Impact on Medical Device Development and Innovation**

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## **Executive Summary**

California is the world's leader in the development of innovative medical technology, and the U.S. Food and Drug Administration (FDA) 510(k) review process is a key regulatory pathway for the introduction of new products. It allows medical device developers to bring new products to market based on data from existing devices, known as predicate devices, that have already been approved as safe and effective. Most important, it is a long-standing, proven mechanism for ensuring timely access to new and improved treatments for patients in need. In the last year alone, 3,000 new devices were approved under the 510(k) process, benefiting physicians and the patients in their care.

Today, the FDA, led by Commissioner Margaret Hamburg, M.D., is weighing material changes to drug and device review. As a result of safety issues raised in the past several years, the FDA has become increasingly focused on risk and sensitive to making sure it fulfills its mission to protect the health and safety of the public. Recently, the agency has engaged in a systemic review of its policies and procedures, including those involved in the clearance of new medical devices under the 510(k) process.

Dr. Jeffrey Shuren, who leads the FDA's Center for Devices & Radiological Health (CDRH), has conducted a series of town hall meetings across the country in an effort to communicate the center's goals and to better understand concerns and perspectives raised by industry, physicians, patients and

consumer groups. Shuren, who previously served as CDRH's acting center director, took over as director in January 2010. His stopovers included visits to Boston, Minneapolis and Irvine (October 2010). Meanwhile, industry has raised concerns that changes to the current 510(k) regulatory pathway could hamper development of innovative medical technologies. CHI, industry groups representing device makers, such as the Medical Device Manufacturers Association (MDMA) and the Advanced Medical Technology Association (AdvaMed), along with investor groups like the National Venture Capital Association (NVCA), have pointed out that a slower, more uncertain FDA review process creates problems for the introduction of life-changing and life-saving products.

Changes to the current process have potential to disrupt the fragile ecosystem that balances academic research, risk capital and the dynamic medical marketplace. Already, many medical device manufacturers have been required by the FDA to conduct larger clinical trials, substantially more data and heightened

post-market surveillance. To highlight current trends in regard to the 510(k) process, on July 29, 2010, CHI convened industry experts, policymakers, academic researchers, former agency officials and industry advocates to discuss the regulatory environment and its potential impact on the medical device industry in California.

### Discussion Highlights

- Escalating media attention driven, in part, by the 24-hour news cycle, has focused mainly on negative stories in which patients suffered harm. This has put safety concerns front and center, and created an increasingly risk-averse environment at the FDA.
- The Institute of Medicine (IOM) recently hosted a series of public workshops in Washington, D.C. to discuss the 510(k) review process and what potential changes are desirable. The institute plans to issue a report by March 2011. Several participants at the CHI event previously made presentations to the IOM.

## Process of 510(k) and Definitions of Class I, II, III

The FDA has established classifications for approximately 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes based on the level of control necessary to assure its safety and efficacy.

### *Class I: General Controls*

Class I medical devices require the least amount of regulatory control, present minimal potential for harm to users and are typically simpler in design and manufacturing than Class II or Class III devices and have a history of safe use. These devices are subject only to general controls, which cover such issues as manufacturer registration with the FDA, good manufacturing techniques, proper branding and labeling, notification of the FDA before marketing the device, and general reporting procedures. Most Class I devices are exempt from good manufacturing practices and/or the FDA notification regulations. Examples of Class I devices include tongue depressors, arm slings, and hand-held surgical instruments.

### *Class II: General Controls with Special Controls*

Class II medical devices are those for which general controls alone are insufficient to assure safety and effectiveness, and additional existing methods are available to provide such assurances. Class II devices are subject to special controls, which may include special labeling requirements, mandatory performance standards and postmarket surveillance in addition to the general controls of Class I devices. Devices in Class II are held to a higher level of assurance than Class I devices, and are designed to perform as indicated without causing injury or harm to patient or user. Devices in this class are typically non-invasive and include: X-ray machines, powered wheelchairs, infusion pumps, surgical drapes, surgical needles and suture material and acupuncture needles.

### *Class III: General Controls and Premarket Approval*

A Class III medical device is one for which insufficient information exists to assure safety and effectiveness solely through the general or special controls sufficient for Class I or Class II devices. Such a device needs premarket approval, a scientific review to ensure the device's safety and effectiveness, in addition to the general controls of Class I. Examples of Class III devices which require a premarket approval include replacement heart valves, silicone gel-filled breast implants, implanted cerebral stimulators and implantable pacemaker pulse generators.

*Source: FDA.gov*

- On Aug. 3, 2010, CDRH released its preliminary internal evaluation and recommendations for changes to the 510(k) process. Among other suggestions, the FDA said it wants to develop guidance clarifying when older devices should not qualify as predicates. It also proposed creating a subset of Class II devices for which clinical or manufacturing data would be needed to bolster an application that compares a new device to an existing one. And the agency also wants to clarify its authority to rescind prior device approvals. (This has only occurred about 100 times since 510(k) rules were adopted in 1976.)

## Setting the Stage

Food and drug regulation in the United States had its roots in the mid-19th century when state and local governments began to enact statutes to protect the public health. Federal regulation began in the early 20th century with enactment of the Food and Drugs Act of 1906. That led to the formal establishment of the regulatory agency known today as the FDA. Today, FDA regulates between one-fifth and one-quarter of U.S. gross domestic product and exerts significant power over the way products enter the market, how they are promoted to consumers and the manufacturing practices of the regulated industry.

In 1938, Congress replaced the 1906 Act with our current law, the Federal Food, Drug, and Cosmetic Act. The 1938 Act for the first time gave FDA authority to regulate medical devices, but it did not provide for any form of premarket review or approval of devices. A significant turning point for the regulation of medical devices occurred in 1962, when Congress first considered legislation to require premarket approval of devices. That legislation was put aside because the thalidomide birth-defect tragedy focused attention on the regulation of new drugs. Congress moved forward with enacting the Drug Amendments of 1962, which required premarket approval of the safety and effectiveness of all new drugs, but it was to be another 14 years before comparable device legislation was enacted.

From 1962 to 1969, medical device legislation was introduced in Congress and endorsed by the president, but no action was taken. In 1969, the U.S. Supreme Court handed down a landmark decision in the United States v. Bacto-Unidisk case, holding that an antibiotic sensitivity disc could be regulated as a drug by FDA. “This woke up the industry, because they realized that FDA

could declare all important new medical devices to be under the new drug provisions of the statute,” said Peter Barton Hutt, who served as the FDA’s chief counsel from 1971 to 1975, and today is partner at the Washington, D.C.-based law firm Covington & Burling LLP. President Nixon convened the Cooper Committee, which published a report that emphasized that devices are different from drugs and require a very different type of regulation by FDA. The Cooper Committee Report recommended the risk-based classification and regulatory system that was enacted into law under the Medical Device Amendments of 1976. Although the 1976 Amendments have been amended several times, the basic structure of that statute remains unaltered. From 1976 on, devices and drugs have been considered categorically different, with separate regulatory pathways for each.

## Legal and Regulatory Perspective: The Current 510(k) Process and Challenges

In recent times, attorneys and regulatory affairs professionals say they have noticed shifts in the FDA’s requirements for approval of new medical devices. Among the many changes noted by Ellen Flannery, an attorney who specializes in food and drug law at Covington & Burling LLP, are requests for additional information and, consequently, longer approval times. For instance, Flannery said it is not unusual for a medical technology company to submit its device based on a predicate as part of the 510(k) process, but for the FDA to reject that claim, saying that the proposed predicate does not apply. Additionally, potential drug/device products are getting shifted over to the FDA’s Office of Combination Products. And more requests for additional information, or AI letters, are being sent to device makers. This, she said, creates an atmosphere of unpredictability and uncertainty in which innovators have no clear idea of what the agency requires or expects of new submissions.

Certainly, transparency initiatives are under way at the FDA and one of the agency’s own stated goals moving forward is to improve predictability. Trade groups representing medical device makers, such as AdvaMed and MDMA, have lauded the FDA for its recognition of this important issue.

David Feigal, former director of CDRH who currently serves as vice president of global regulatory affairs at Amgen, also

broached the issue of predictability and its impact on medical technology device development. He referred to unpredictability as an “innovation inhibitor.” Without standards for review, device makers have difficulty bringing their products to the market, he said. His talk provoked a key question: “How do we foster innovation in this very large area of Class II medical devices?” Most medical devices belong to this class, which can be subject to special controls beyond the general controls of Class I devices (see sidebar on page 2).

**“The innovation inhibitors** are when the regulatory requirements become burdensome or when the review cycles become longer. The challenge at FDA is that there are 15 new 510(k)s to approve every day to stay in steady state.”

*David Feigal, M.D.  
Vice President, Global Regulatory Affairs, Amgen  
Former Director of the Center for Devices &  
Radiological Health*

Among other suggestions for encouraging innovation while ensuring that devices are safe and effective, Feigal proposed that device classification should take into account individual technologies rather than categorizing technologies broadly under one umbrella. He pointed to ultrasound device classification as an example. “One set of regulatory requirements does not fit all,” he said.

### Discussion Highlights:

- The FDA’s data indicate that it receives about 3,000 510(k) submissions each year, with 85 percent considered devices that are substantially equivalent to devices already on the market. About 10 percent are withdrawn or are determined to be something other than a device. The rest (about 5 percent) are devices not considered substantially equivalent. (Flannery)
- Those so-called problem devices, according to Flannery, are “usually the novel ones, the innovative ones, the things that really have the potential to advance the public health.”
- Only a small percentage of 510(k)s require clinical data to support the application, but for those device makers that might need an Investigational Device Exemption (IDE) to

conduct clinical trials, pre-IDE discussions with the FDA are taking significantly longer.

- Clinical trial sizes have also been influenced by recent FDA decisions. Flannery said she’s seen FDA requests for larger trials, especially for devices that provide only a marginal benefit over existing products.
- There also is a standard operating procedure (SOP) for resolution of internal differences of opinion at FDA. This guarantees a reviewer has a voice if he or she is disputing a decision with the rest of the review team. This process can also slow a device from entering the market.

## Industry Perspective: Regulatory Trends and Implications for Biomedical Innovation and Public Health in California

### Issue at a Glance:

The medical device ecosystem relies on a series of participants who all play important roles in bringing new devices to the market and into the hands of physicians and patients. Dr. Josh Makower, chief executive and founder of the Mountain View, Calif.-based incubator ExploraMed Development LLC, best describes this as beginning with the “fuelers,” or those who fund development of early-stage ideas, and concluding with regulatory approval and market introduction. In between are the small startups and entrepreneurs with promising new ideas and the potential to change medical practices. A key step toward achieving some of these ambitious goals involves navigating the U.S. regulatory process. The FDA’s 510(k) process, according to Makower, is “a way to build upon existing bodies of knowledge

**“The medical device industry** is already under tremendous pressure from multiple sources. Putting the 510(k) process at risk is the straw that could break the camel’s back and the impact on medical innovation and the advancement to patient care could be devastating.”

*Josh Makower, M.D.  
CEO and Founder, ExploraMed Development LLC*

and introduce what are essentially incremental innovations that build on that foundation and introduce modifications that truly can deliver better outcomes for patients. If these regulatory processes become too uncertain, unpredictable or unnecessarily burdensome, they will deter even the most talented and creative innovators from even entering the system. This has severe implications for patients and for our economy.”

**“An overly burdensome** regulatory system may constrain one of the great industries in America, one of the great export industries and one of the great advancers of healthcare around the globe.”

*Robert “Chip” Hance  
 President, Abbott Vascular*

**Discussion Highlights:**

Laparoscopic devices transformed surgery and intravascular ultrasound, or IVUS, revealed an underlying mechanism that improved the outcome for stenting. These are just two examples of how medical devices transformed the practice of medicine and led to better patient treatment and improved outcomes. Before a new device has the chance to reach the market, however, device makers must not only find funding, they must also navigate a sometimes complex set of approval processes. In recent times, device makers say they have noticed a shift in terms of FDA focus during the review process. “Questions about the rigor of the 510(k) path to market are prompting an increasingly conservative approach,” said Robert “Chip” Hance, who serves as president of Abbott Vascular. “The breadth and depth of regulatory requirements are increasing, driving longer cycle times and higher development costs.”

Hance referred to this transformation as moving toward a “rule-based” rather than a “risk-based” approach, which has been the standard until recently.

“In order to advance innovation, we need to make the process more predictable and give applicants a better sense of the rules of the road, including consistent approval standards, more detailed guidance on predicate devices and requirements for product clearance, and greater transparency of data requirements.”

Much of the shift in focus has to do with emphasis on risk versus innovation at the FDA, according to Peter Barton Hutt. Depending on extenuating circumstances, such as major recalls,

Hutt says there are cyclical increases or decreases in requirements of device makers by FDA. The panelists agreed that the current cycle is trending toward increased requirements and an emphasis on risk as opposed to benefit. Historically, device makers justified a research and development program based on the ability to achieve success in the United States. Today, Hance said Abbott Vascular finds itself looking to international markets to launch products, where barriers to entry are less stringent. “That’s a sea change for this entire California-based medical device industry,” he said.

**Does Recall Data Suggest a Fundamental Flaw in the 510(k) Process?**

**Key Question:**

Does the 510(k) review system permit products onto the market without a “reasonable assurance of safety and effectiveness?”

**Introduction:**

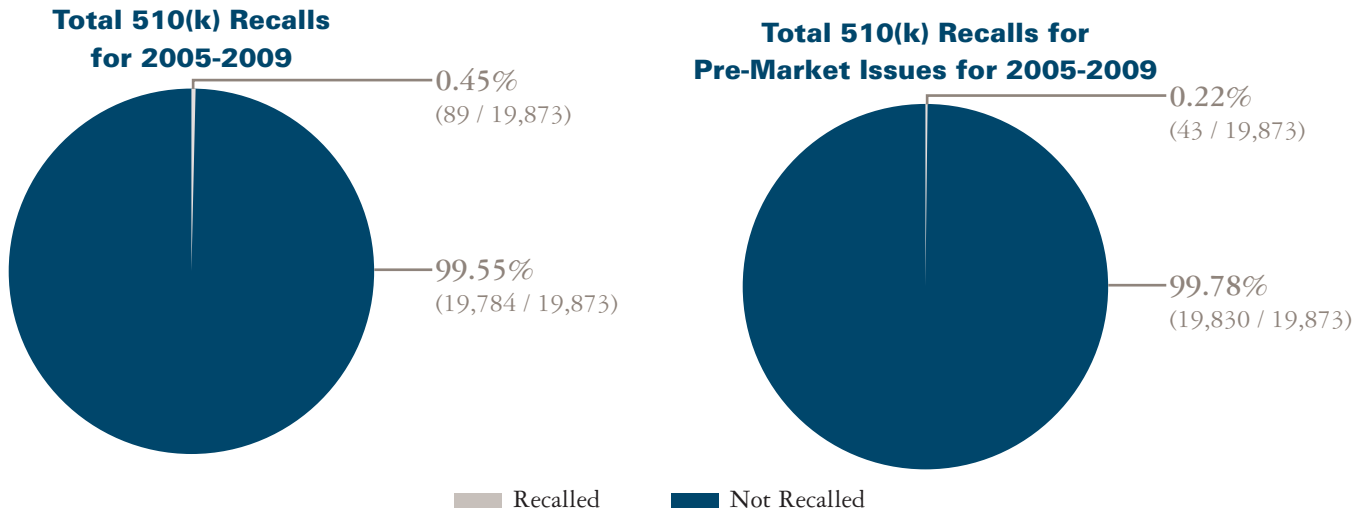
In an effort to better understand and gain insight into the robustness of the 510(k) program from a safety perspective, Ralph Hall, Counsel, Baker & Daniels LLP and CEO MR3 Medical LLC, set out to gather data on medical device recalls over a five-year period, from 2005 to 2009. In all, his data reflected 474 total recalls, of which 118 were stand-alone Class I recalls (see sidebar on page 7) that formed the basis of his report. He noted that while the 510(k) review system has been subjected to a fair amount of criticism, there was a lack of systemic data to support critics’ claims. “If we’re allowing unsafe products on the market, we need to do something,” Hall said. “If we’re not seeing a safety problem, the reasons to change the system may be administrative, bureaucratic ease, other things, but they’re not safety issues.” To gather the relevant facts, Hall spent five months

**“Policy should be driven** by facts and data as compared to opinion and anecdote.”

*Ralph Hall  
 Law Professor, University of Minnesota  
 Counsel, Baker & Daniels LLP  
 CEO, MR3 Medical LLC*

**Very Few 510(k) Clearances Have Been Subject to a Class I Recall**

Hall's data show that less than one percent of devices that were cleared by the 510(k) process had been recalled. He found a total of 89 recalls in a five-year period out of an average of 19,873 submissions.



Total 510(k) Approvals in 10 years	39,747
Average Submissions in 5-year time period	19,873
Total 510(k) Recalls for 2005-2009	89
Total 510(k) Recalls for Pre-Market Issues for 2005-2009	43

researching public databases and speaking with companies to produce a comprehensive report that he presented to the IOM, and, subsequently, shared at the CHI program. His research was supported by a grant from the Kauffman Foundation, and backed by the University of Minnesota.

Among the notable findings, Hall's study discovered that very few 510(k) clearances have been subject to a Class I recall, which represents the highest safety risk. In fact, fewer than one percent (0.45 percent) of products submitted through this regulatory process had been recalled. Hall culled data from FDA databases, the 2009 Government Accountability Office (GAO) report and related materials, Internet queries and interviews with companies and the FDA.

To his surprise, Hall found that there was no statistically significant difference in the number of 510(k) and pre-market approval (PMA) device recalls. Design issues (including software design) were identified as the predominate reason for the recall of devices that had been cleared by FDA through 510(k). Hall

suggested that the role of bench testing and design controls (also called Quality Systems Regulation) rather than additional clinical trials would best address any issues.

Hall also categorized his recall research by product type, to determine whether certain product categories accounted for a disproportionate share of Class I recalls. He discovered that two kinds of products – automated external defibrillators and infusion pumps – accounted for 28 percent of all recalls during the five-year period. This led Hall to ask: “Does this drive us toward more product-type specific changes or does this drive us more toward changing the overall process?” He noted that the FDA already has initiatives in place to address infusion pump safety issues. Remarkably few recalls were for orthopedic or obstetrics and gynecology products, he added.

In summary, Hall noted a lack of recalls related to premarket issues and questioned the use of additional clinical trials and a proposed fourth device classification based on safety profiles.

## Conclusion

The 510(k) process is a mechanism integral to medical technology innovation. As the day's proceedings demonstrated, however, increased uncertainty, unpredictability and inconsistency are beginning to take a toll. As the FDA, IOM and Congress consider reforms to 510(k), including some viewed as controversial—restricting use of multiple and split predicates, consolidating concepts of “indication for use” and “intended use,” creation of a subset of Class II devices, rescission authority, etc.—careful and deliberative consideration must be given to ensure that the process does not become more cumbersome, complex and costly, to the detriment of medical technology investment, innovation, and, ultimately, patient care.

## Partnering with CHI

CHI-California Healthcare Institute is working to ensure that FDA's 510(k) review process takes into account the views and perspectives of California's innovative medical technology sector, so that changes to 510(k) should promote predictability and

consistency in the process, and not, without sound justification, add additional requirements or burdens to the detriment of medical technology investment and innovation.

CHI welcomes your participation in future discussions on the regulatory environment and medical device innovation. Contact Todd Gillenwater, vice president of public policy for CHI, at 202-974-6313 or [gillenwater@chi.org](mailto:gillenwater@chi.org) for more information on how to get involved, or visit the CHI website at [www.chi.org](http://www.chi.org).

## Resources

Center for Devices and Radiological Health 510(k) Information:  
<http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHReports/ucm220272.htm>

Institute of Medicine 510(k) Hearings:  
<http://www.iom.edu/Activities/PublicHealth/510KProcess.aspx>

AdvaMed 510(k) Action/Opinion:  
<http://www.advamed.org/MemberPortal/Issues/FDA/>

Medical Device Manufacturers Association 510(k) Action/Opinion:  
<http://www.medicaldevices.org/issues/FDA>



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