

# Regulatory Strategy Forum for Medical Devices

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## Hot Topics: 510(k) Reform

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## 510(k) and Science Reports

- ❖ **Don't panic!**
- ❖ **Draft reports published: August 5, 2010**
  - Comment Period closed: October 4, 2010
- ❖ **55 Recommendations from both reports**
- ❖ **Center is currently prioritizing recommendations**
- ❖ **After comments are evaluated, a determination will be made regarding which recommendations to implement and which should wait until after the IOM report**
- ❖ **Recommendations will go through notice as comment as appropriate**





# Notable Recommendations

## Improving Patient Safety

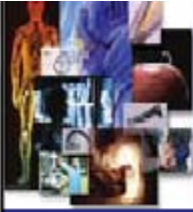
- ❖ Revise regulations to explicitly require 510(k) submitters to provide a summary of **all scientific information known** or that the submitter should reasonably know regarding the safety and effectiveness of the device under review. This is not required now for 510(k) submissions and, as a result, relevant information may not be included in an initial submission. This summary would help CDRH review staff to more efficiently make decisions, and potentially avoid extensive follow-up inquiries and questions.
- ❖ Develop a guidance document that clarifies **when a device should not be used as a predicate**, such as when the device has been removed from the market because of safety concerns. The report also recommends that the center consider issuing a regulation that would clarify the circumstances under which the center would exercise its authority to rescind a 510(k) clearance to remove an unsafe device from the market and preclude its use as a predicate and also consider whether additional authority is needed.
- ❖ Build upon **public databases** to include meaningful, up-to-date information that supports good decision making and promotes the safe use of devices. This could be accomplished by improving the current 510(k) database so that it includes summaries of FDA review decisions, current labeling and photos.



# Notable Recommendations

## Fostering Device Innovation

- ❖ The 510(k) report recommends major improvements to the regulatory pathway for lower-risk novel devices that cannot be cleared through 510(k) but which do not warrant the more rigorous premarket approval review applied to higher-risk devices. The report calls for major reforms in the implementation of this process – called the **de novo classification process**. The recommendations include streamlining the process and clarification of CDRH's expectations for submissions that undergo this type of review.
- ❖ The science report recommends that CDRH make better use of scientific experts outside of the agency by developing a web-based network of **external experts** using social media technology. This network would help CDRH staff leverage outside knowledge without serving in an advisory capacity.



# Notable Recommendations

## Enhancing Regulatory Predictability

- ❖ Develop a guidance document defining a subset of moderate-risk (Class II) devices, called **Class IIb**, for which clinical or manufacturing data typically would be necessary to support a substantial equivalence determination. This guidance document would help clarify what information submitters should include in their 510(k) submissions so that they can plan accordingly. In addition, this would also help the center's review staff obtain the type and level of evidence necessary to make well-supported decisions without as much need for time-consuming follow-up requests for information.
- ❖ The science report recommends use of a standardized "**Notice to Industry**" letter that would generally be issued as a "Level 1 - Immediately in Effect" guidance document to quickly communicate when CDRH has changed its premarket regulatory expectations due to scientific information that has emerged about a certain device type. CDRH currently communicates this kind of information through individual interactions during the review process, which can lead to delays. These letters would provide greater clarity to affected manufacturers, in a timelier manner, about CDRH's expectations with respect to a particular group of devices.



## General Comments

- ❖ **CDRH should not implement all recommendations at once**
- ❖ **Notice and comment should be allowed once detailed recommendations are developed**
- ❖ **Innovation should not be hindered by proposed changes**
- ❖ **510(k) should be improved to provide greater consumer protection**



## Recommendations with strong support

- ❖ **Revise the de novo process**
- ❖ **Improve the guidance process**
- ❖ **Issue guidance in a number of areas**
  - o Clarify technological characteristics
  - o Clarify the difference between intended use and indications for use
- ❖ **Training**
- ❖ **Access to external expertise and establish a science counsel**



# Recommendations with mixed support

## ❖ Periodic reports

### ❖ Class IIb

- o Initial comments before the report issued supported concept
- o Comments now are less supportive

### ❖ Rescission

- o Industry comments are not supportive, or are supportive only in cases of fraud
- o Other stakeholders are supportive

### ❖ Predicates

- o Guidance on use of predicates
- o Restrictions on split predicates



## Recommendations with significant concern

- ❖ **Posting pictures or schematics of the device**
- ❖ **Combining Intended Use and Indications for Use**
  - o Clarify but don't combine
  - o "Fear" that products must be identical
- ❖ **Statutory authority for off-label use**
- ❖ **Manufacturing information/pre-clearance inspections**



# Rescission

**The recommendation on rescission is not intended to add any authorities over what the agency believes are currently existing. It is intended to provide transparency and predictability by:**

- o Assuring the 510(k) holder due process rights;
- o Providing the 510(k) holder an opportunity for an informal hearing before issuing a rescission order; and
- o Issuing a regulation providing the 510(k) holder with the opportunity to request a hearing to challenge a proposed withdrawal.



## Class IIb

- ❖ **Intended to provide predictability**
  - o Identify data needs based on existing review requirements
- ❖ **Intended to be fluid**
  - o Devices could move off of the list
- ❖ **Provide a level of harmonization**
- ❖ **Intended to apply to the broad category of existing Class II devices**



## Providing All Readily Known Information

- ❖ **Comments are mixed:**
  - o Some disagree due to burden
  - o Some think it should be applied to certain device types
  - o Some are supportive and feel that FDA reviewers should not have to play Where's Waldo





# Multiple Predicates



## New Device



## Predicates





# Split Predicates



## ❖ New Device

- o Low Energy Ultrasound Wound Cleaner

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## ❖ Most Appropriate Pathway

### De Novo

- o Based on well understood technology it is possible to write special controls to support a Class II classification

## ❖ Predicate Devices

- o Wound Flush Solution Class II
  - Intended Use
  
- o Ultrasound and muscle stimulator for use in applying therapeutic deep heat for selected medical conditions Class II
  - Technology



# IOM

- ❖ **The committee will assess whether the 510(k) clearance process sufficiently protects patients and promotes public health. Specifically, the IOM committee will answer two principal questions:**
  - Does the current 510(k) process optimally protect patients and promote innovation in support of public health?
  - If not, what legislative, regulatory, or administrative changes are recommended to optimally achieve the goals of the 510(k) process?
  
- ❖ **A report is expected in mid-2011.**

# So What Happened?

- FDA held 2 public meetings and 3 town hall meetings, 3 open public dockets and many individual stakeholder meetings
- 76 comments submitted from diverse stakeholder groups
- FDA issued Summary and Overview of Comments and Next Steps document on January 19, 2011
- Of the original 55 recommendations:
  - 28 received overall support
  - 12 received support with modification or caveat
  - 15 received significant concern

# Recommendations Being Pursued

- FDA plans to implement recommendations that received overall support or support with modification/caveat
- Focus on actions with greatest impact on fostering medical device innovation, enhancing predictability, and improving patient safety:
  - Streamlining the de novo process
  - Issuing guidance to improve clarity about 510(k) program
  - Improving training for CDRH staff and industry
  - Make greater use of external experts
  - Make critical business process improvements in CDRH
  - Establish a Center Science Council

# Received Support

- Strengthen training, staffing, retention, business processes
- Strengthen internal processes for decision making, incorporating new scientific info, etc.
- Issue clinical trials guidance and build internal expertise
- Issue guidance on use of consensus standards and documentation within a 510(k)
- Issue guidance on requests for clinical data in support of a 510(k)
- Implement UDI
- Develop guidance and SOPs on use of product codes
- Issue guidance and SOPs on 510(k) Summaries
- Issue guidance and regulations regarding transfer of 510(k) ownership

# Received Qualified Support

- Revise “least burdensome” guidance – not intended to lower expectations with respect to what is necessary to demonstrate a device meets the relevant statutory standard
  - In lieu of revising guidance, will train review staff and industry
- Develop social-media based network of external experts
  - Will develop SOP on engagement with external experts
- Issue “Notice of Industry” letters when regulatory expectations change
  - Will develop SOP to clarify parameters for issuing these letters
- Continued use of Transparency website (e.g., summaries of review decisions not currently made public)
  - Will not include confidential or proprietary information

# Received Qualified Support (continued)

- Reconcile language and issue guidance on “different technological characteristics” and “different questions of safety and effectiveness”
  - Will provide guidance and interpretations consistent with Act
- Streamline de novo process and evidentiary expectations
  - Will clearly delineate eligibility criteria
- Clarify when device modifications require a new 510(k), and when a Special 510(k) is appropriate
  - Will issue guidance to provide greater clarity
- Submission of detailed photographs and schematics
  - Will clarify steps taken to assure confidentiality

# Received Qualified Support (continued)

- Clarify statutory listing requirement on device labeling
  - Submit current labeling annually with device listing
- Regularly update list of devices eligible for third party review
  - Update SOP for identifying devices eligible for third party review
- Periodic audit of 510(k) revision decisions
  - Will not be used to reverse previous 510(k) determinations for marketed products

# Controversial Provisions to be Implemented with Modifications

- Online labeling repository
  - Will hold public meeting prior to implementing a scaled-back version that addresses public comments
  - May link to manufacturer's websites with posted labeling
- Assurance case framework
  - To be piloted for infusion pumps
- Public database with device photograph
  - Concern with proprietary information
  - Will hold public meeting and address public comments

# To Be Implemented on a Case-by-Case Basis

- Requiring regular, periodic updates of device modifications
- Requiring submission of a list and brief description of all scientific information related to the safety and effectiveness of a new device known or reasonably known to the submitter
  - Through device-specific guidance; clarify to information “already known” to the submitter
- Requiring manufacturing data to be submitted in a 510(k)
- Clarifying when CDRH will withhold clearance for failure to comply with GMP’s and require a pre-clearance inspection

# Recommendations On Hold Pending IOM Feedback

- Consolidate terms “indications for use” and “intended use”
  - Could inadvertently be disincentive to new indications
- Consider off-label use when determining intended use
  - Focus on situations where the primary use is expected to be off-label
- Issue guidance on when a device should no longer be available for use as a predicate
  - Rescission may be option
- Issue a regulation on rescission authority
  - FDA believes it has the authority under appropriate circumstances

# Recommendations On Hold Pending IOM Feedback

- Require manufacturers to keep one unit of a device available
  - May be impractical for large devices, and may not be available at time of submission
- Issue guidance to create a “Class IIb”
  - One of the most controversial proposals
  - Would clarify requirements for clinical, manufacturing or postmarket data for higher risk Class II devices
- Require postmarket surveillance studies as a condition of clearance for certain devices
  - Concern that would be duplicative of existing requirements and burdensome

# Abandoned: Split Predicates

- As described, CDRH's definition of split predicates was inconsistent with the applicable provisions in the Act
- Semantic issue...no change planned
- Instead will issue guidance to clarify use of multiple predicates
- CDRH "strongly supports" the use of multiple predicates

# Next Steps

- Plan for 25 actions released mid-January
- Individual notice and comment periods (e.g., for new draft guidance documents)
- Issue device-specific guidance where applicable
- Public Meeting April 7-8, 2011
  - Public posting of device photographs
  - Development of online labeling repository

# Timetable (1)

DESCRIPTION	ACTION	PURPOSE	MILESTONE	DATE OF COMPLETION
GUIDANCE	510(k) Modifications Guidance	To clarify which changes do or do not warrant submission of a new 510(k) and which modifications are eligible for a Special 510(k).	Draft Guidance	June 15, 2011
	Clinical Trial Guidance	To improve the quality and performance of clinical trials.	Draft Guidance	July 31, 2011
	Evaluation of Automatic Class III Designation (De Novo) Guidance	To streamline the de novo classification process.	Draft Guidance	September 30, 2011
	Standards Guidance	To clarify the appropriate use of consensus standards.	Draft Guidance	October 31, 2011
	Appeals Guidance	To clarify the process for appealing CDRH decisions, including decisions to rescind a 510(k).	Draft Guidance	October 31, 2011
	510(k) Paradigm Guidance	To provide greater clarity regarding: 1) when clinical data should be submitted in support of a 510(k); 2) the submission of photographs or schematics for internal FDA use only; 3) the appropriate use of multiple predicates; 4) the criteria for identifying "different questions of safety and effectiveness" and technological changes that generally raise such questions; 5) resolving discrepancies between the 510(k) flowchart and the Food, Drug, and Cosmetic Act; 6) the characteristics that should be included in the concept of "intended use"; and 7) the development of 510(k) summaries to assure they are accurate and include all required information.	Draft Guidance	September 30, 2011
	Pre-Submission Interactions Guidance	To supplement available guidance on pre-IDE meetings and enhance the quality of pre-submission interactions between industry and Center staff.	Draft Guidance	November 30, 2011
	Product Code Guidance	To more consistently develop and assign unique product codes.	Draft Guidance	December 31, 2011

# Timetable (2)

			MILESTONE	DATE OF COMPLETION
INTERNAL and ADMINISTRATIVE MATTERS	Establish a Center Science Council	To: 1) oversee the development of a business process and SOP for determining and implementing an appropriate response to new scientific information; 2) promote the development of improved metrics to continuously assess the quality, consistency and effectiveness of the 510(k) program; 3) periodically audit 510(k) review decisions to assess adequacy, accuracy and consistency; and 4) establish an internal team of clinical trial experts to provide support and advice on clinical trial design for Center staff and prospective IDE applicants.	Post Council Charter to FDA Website	March 31, 2011
			Post initial results of 510(k) audit to FDA Website	June 15, 2011
	Assess Center Staffing Needs	To formalize the Center's internal process for identifying staffing needs, and to enhance recruitment, retention, training, and professional development of review staff.  To create a mechanism to assemble an experienced ad hoc team to temporarily assist with unexpected surges in workload.	Develop process for identifying, recruiting, retaining, and training needed staff	July 15, 2011
	Enhance Training	To train new Center staff on core competencies.  To train Center staff and industry on: 1) the determination of "intended use"; 2) the determination of whether a 510(k) raises "different questions of safety and effectiveness"; 3) the review of 510(k)s that use "multiple predicates"; 4) the development and assignment of product codes; 5) the interpretation of the "least burdensome" principles; and 6) the appropriate use of consensus standards.	Develop and implement training on core competencies	August 31, 2011
	Leverage External Experts	To develop a network of external experts to appropriately and efficiently leverage external scientific expertise. Also, to assess best-practices and develop SOPs for staff engagement with external experts.	Post SOP to FDA Website	September 15, 2011
	Continue Integration and Knowledge Management	To improve knowledge management across the Center.	Complete evaluation of methods used to integrate device information into a dynamic format so that it can be more readily used by staff to make regulatory decisions	September 30, 2011

# Timetable (3)

			MILESTONE	DATE OF COMPLETION
PROGRAMMATIC and REGULATORY	Implement an "Assurance Case" Pilot Program	To explore the use of an "assurance case" framework for 510(k) submissions.	Start pilot program	March 31, 2011
	Provide Additional Information About Regulated Products	To make device photographs available in a public database without disclosing proprietary information.	Public Meeting *	April 7 - 8, 2011 *
	Improve Collection and Analysis of Postmarket Information	To develop better data sources, methods and tools for collecting and analyzing meaningful postmarket information, and to enhance the Center's capabilities to support evidence synthesis and quantitative decision making.	Determine system requirements and select the platform for a new adverse event database	June 30, 2011
	Establish "Notice to Industry Letters" as a Standard Practice	To clarify and more quickly inform stakeholders when CDRH has changed its regulatory expectations on the basis of new scientific information.	Post SOP to FDA Website	June 15, 2011
	Improve the IDE Process	To better characterize the root causes of existing challenges and trends in IDE decision making.	Complete program assessment	June 30, 2011
		Assess, characterize and mitigate challenges in reviewing IDE's.		
	Implement a Unique Device Identification (UDI) System	To permit the rapid and accurate identification of devices, to facilitate and improve adverse event reporting and identification of device-specific problems.	Issue proposed regulation	June 30, 2011
	Multiple Predicate Analysis	To conduct additional analyses to determine the basis for the apparent association between citing more than five predicates and a greater mean rate of adverse event reports.	Complete analysis and make results public	October 31, 2011

# Timetable (4)

			MILESTONE	DATE OF COMPLETION
PROGRAMMATIC and REGULATORY (cont.)	Clarify and Improve Third-Party Review	To develop a process for regularly evaluating the list of device types eligible for third-party review and to enhance third-party reviewer training.	Post SOP to FDA Website	September 30, 2011
	Streamline Guidance and Regulation Development Process	To provide greater clarity, predictability, and efficiency in the guidance and regulation development process.	Post SOPs to FDA Website	July 31, 2011
	Draft 510(k) Transfer of Ownership Regulation	To better document 510(k) transfers of ownership.	Issue proposed regulation	December 31, 2011
	Improve Medical Device Labeling	To develop an on-line labeling repository.	Public Meeting *	April 7 - 8, 2011 *
		To clarify the statutory listing requirements for the submission of labeling.	Issue proposed regulation	December 31, 2011

# Timetable (5)

DESCRIPTION	ACTION	PURPOSE	MILESTONE	DATE OF COMPLETION
ISSUES TO BE REFERRED TO THE IOM	Rescission Authority	To consider defining the scope and grounds for the exercise of the Center's authority to fully or partially rescind a 510(k) clearance.	IOM REPORT	SUMMER 2011
	Postmarket Surveillance Authorities	To seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices.		
	Establish a Class IIb	To develop guidance defining "class IIb" 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.		
	Predicate Clarification	To clarify when a device should no longer be available for use as a predicate.		
	Clarify and Consolidate Regulatory Terms	To consolidate the concepts of "indication for use" and "intended use" into a single term, "intended use".		
	Device Review	To consider the possibility of requiring each 510(k) submitter to keep at least one unit of the device under review available for CDRH to access upon request.		
	Off-Label Use	To explore the possibility of pursuing a statutory amendment that would provide the agency with the express authority to consider an off-label use when determining the "intended use" of a device.		

\* The April 7-8, 2011 meeting will discuss both actions.

# Questions

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