Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
No specific text in Forward	Page 11, Item 2, cont, Quality of Submissions: Improper Use of Recognized Standards	Such a requirement could substantially increase the reviewers' work load.
	Page 6, 1.1 Overview / Findings and Recommendations, 2nd complete paragraph – " , , , recommends that CDRH develop program metrics and better systems for continuous monitoring of 510(k) program performance and effectiveness . . ." Page 14 – 15, Item 2, cont, Continuous Quality Assurance	The 510(k) process is in need of management engagement, oversight and monitoring to meaningful metrics. Over recent years, ODE managers seem to have moved away from exerting managerial oversight for staff reviews of subordinate personnel or organizations. Thus, training should be accompanied by re-empowering managers to exert oversight and then holding managers accountable for reviews conducted within their supervisory authority. Reviewer training needs to show balanced attention to the role of science and to the role of law, regulations, policies, established practices, and precedence. Monitoring the 510(k) program in the form of management reviews and audits of 510(k) decisions to defined program metrics is a fundamental requirement for instilling a means for continuous improvement.

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October 4, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. FDA-2010-N-0348

King & Spalding LLP's Comments Regarding the Center for Devices and Radiological Health's Preliminary Internal Evaluations of the 510(k) Process and the Use of Science in Regulatory Decision Making

Dear Sir or Madam:

The table attached to this letter contains King & Spalding LLP's comments regarding the Center for Devices and Radiological Health's ("CDRH") *"510(k) Working Group Preliminary Report and Recommendations"* ("the 510(k) Report") and CDRH's *"Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations"* ("the New Science Report"), both of which the Food and Drug Administration'("FDA" or "the Agency") issued on August 4, 2010. We are submitting these comments electronically by the October 4, 2010, 11:59 p.m. ET deadline set forth in 75 Fed. Reg. 43707 (August 5, 2010). Therefore, we request that FDA include this letter and the attached table in **Docket No. FDA-2010-N-0348**, which pertain to those reports. We also request that the Agency review and consider our comments before deciding which recommendations to implement.

We applaud FDA's efforts to make the 510(k) process more predictable, consistent, and efficient while retaining the flexibility to adapt to new technologies and new uses of, changes to, and new information about, existing technologies, which FDA describes as being "predictably adaptive." We agree with FDA that predictable adaptability is the best approach for meeting the two goals of the 510(k) process, which are as follows: (1) making available to consumers devices that are safe and effective; and (2) fostering innovation in the medical device industry. For this reason, we support the recommendations in the 510(k) and New Science Reports that we believe would increase FDA's predictable adaptability and thus, further both goals of the 510(k) process. We do, however, have concerns about some of the changes FDA is proposing. We believe that some of FDA's proposed changes would undermine the 510(k) process, would not help FDA respond to new scientific information or to respond in a beneficial manner, or are unnecessary, unduly burdensome, or unworkable. We have therefore suggested some modifications or identified areas of concern that we urge FDA to address before implementing any changes.

The attached table contains our comments. All of our comments are based on our communications with the device industry and our device regulatory experience. We trust that FDA will find our comments informative.

If you have any questions regarding our comments, please contact me at (202) 626-2903 or at EBasile@KSlaw.com. We look forward to FDA's identification of the recommended changes that the Agency proposes to implement and the issuance of guidance, standard operating procedures, policies, and other documents that contain more detailed information about the proposed changes.

Sincerely,

Edward M. Basile

Edward M. Basile

Attachment: King & Spalding LLP's Comments

cc: Laurie A. Clarke, King & Spalding LLP
Lynette Zentgraft, King & Spalding LLP

Docket No. FDA-2010-N-0348

FDA's Preliminary Evaluation of the 510(k) Process and the Use of New Science in Device Regulation

This table summarizes the recommendations set forth in the Food and Drug Administration's ("FDA" or "the Agency") "*510(k) Working Group Preliminary Report and Recommendations*" ("the 510(k) Report") and the Agency's "*Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations*" ("the Science Report"). This table also summarizes the 510(k) Working Group and New Science Task Force's (collectively "the FDA Internal Committees") stated rationales for their recommendations. In addition, the table contains King & Spalding LLP's ("King & Spalding") analysis of the potential impact(s) of each of the FDA Internal Committees' recommendations, if the Agency implements it, and comments regarding whether and to what extent the firm supports the recommendations.

The FDA Internal Committees' Recommendations	**The FDA Internal Committees' Stated Rationales for Their Recommendations**	**King & Spalding's Views on Potential Impact of the Recommendations, if Implemented**	**King & Spalding's Comments on the Recommendations**
The FDA WORKING GROUP'S 510(k) REPORT			
Rational, Well-Defined, Consistently Interpreted Review Standard			
Clarify meaning of "substantial equivalence"	Insufficient clarity for key terms in the definition of "substantial equivalence," namely, "same intended use" and "different questions of safety and effectiveness."	While we support clarification of these definitions, we would strongly oppose any efforts to narrow these definitions as it would limit the number of devices that could be cleared through the 510(k) process.	
➢ "Same Intended Use"			
• *Lack of a clear distinction between terms*: Consolidate "indication for use" and "intended use" into a single term, after careful consideration to avoid incorrectly categorizing certain changes currently part of the indications for use as changes to intended use. CDRH should also carefully consider how it will rename the "Indications for Use" statement and form.	The difference between the two terms is unclear which "has led to a lack of clarity about what reviewers should consider in determining whether or not a new device has the same 'intended use' as the predicate to which it is compared." Merging the terms would lead to greater consistency in interpretation and application.	Under 21 U.S.C. 513(i)(1)(a)(i) and 21 C.F.R 807.100(b)(1), a new device must have the same intended use as its predicate device(s) to be found substantially equivalent to it/them. The impact the consolidation of these terms would largely depend on how FDA defines "intended use". The 510(k) report states that FDA does not intend for modifications that are currently considered to be only changes in indications for use to constitute a new intended use.	We urge FDA to retain both terms because they serve different purposes. • A device's indications for use are the uses for which: (1) FDA has cleared the device; (2) FDA has exempted the generic type of device from 510(k) requirements; (3) FDA has stated it will exercise its enforcement discretion and not regulate the device for; or (4) the uses of a device

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The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
		However, FDA has not yet proposed a definition of intended use, so it is unclear what differences would constitute a new intended use. We would strongly oppose any definition of intended use that would result in more devices being found not substantially equivalent ("NSE") and thus, requiring approval of premarket approval applications ("PMA").	before the May 28, 1976, enactment of the Medical Device Amendments of 1976 for devices marketed before that date. The indications for devices cleared since FDA began requiring indications for use statements in 1996, are listed on their indications for use statements enclosed with their substantial equivalence letters. A device's indications are the uses for which it may be legally marketed and thus, for which it may be labeled and promoted. • A device's intended use is its general therapeutic, diagnostic, etc., effect that is derived from its indications for use. The purpose of a device's intended use is to determine whether it can be found substantially equivalent to a predicate device or requires approval of a PMA. FDA has, in effect, acknowledged that continuing need to identify a device's cleared uses, for the Agency wants to retain, but rename, the indications for use statement. The retention of both terms reduces the risk that differences between a new device and its predicate devices'

The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
			indications that do not alter the intended therapeutic, diagnostic etc., effect of the device or impact the safety or effectiveness of that effect would nevertheless be considered different intended uses and thus, the new device would require PMA approval. This approach is based on FDA's long-standing policies set forth in the Agency Guidance entitled "*Guidance on the CDRH Premarket Notification Review Program*", 510(k) Memorandum #K86-3 (June 30, 1986), which is commonly called the "Mohan Memorandum." Furthermore, it would be both easier to administer and less confusing than try to merge parts of a device's indications into its intended use and create a new term for the parts of the indications that are not included in its intended use. However, we believe it is necessary to define these terms as set forth above to clarify their respective purposes and how they relate to each other because, as FDA admits, the Agency and Industry have sometimes used them interchangeably. We encourage FDA to identify the required and optional elements of a device's indications for use and to create an indications template that companies can use to identify a device's proposed indications. Alternatively, if FDA retains only the

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			"intended use" term, we request that the Agency define this term to mean the general therapeutic, diagnostic, etc., effect or purpose of the device and not the information currently included only in a device's indications for use statement.
• *Insufficient guidance for 510(k) staff and industry*: Develop or revise existing guidance and training programs for reviewers, managers, and industry to clearly identify what constitutes "intended use."	Existing CDRH guidance documents and training programs "do not provide enough direction to allow for consistent implementation of 'intended use' criteria."	Guidance on the meaning of "intended use" and what it includes would help FDA reviewers and industry determine whether a new device has the same intended use as its predicate device(s).	We support FDA's providing new or updated guidance to the Agency Staff and the public regarding the term "intended use", so long as this guidance would not result in more devices being found NSE.
• *Off-label use*: Pursue a statutory amendment to the Federal Food, Drug, and Cosmetic Act ("FDC Act") giving CDRH "express authority to consider an off-label use, under certain limited circumstances, when determining the 'intended use'" of a 510(k) device. If CDRH does so, it should define what evidence would be needed to determine that the true primary intended use is an off-label use.	Sometimes, a device's true primary "intended use" may in fact be an off-label use and CDRH could clear a device without considering the safety and efficacy of that off-label "intended use."	This change would require device manufactures try to identify potential off-label use of a device, predict off-label uses that FDA would be concerned about, if any, provide data to support such uses even if they do not intend for the device to be used for that purpose, or modify the device to prevent such use. If FDA tries to prevent off-label use, the Agency risks interfering with the practice of medicine.	We oppose an expansion of FDA's authority to consider off-label uses when reviewing a 510(k) notice. FDA currently has the authority under Section 513(i)(1)(E) of the Food, Drug, and Cosmetic Act ("FDC Act") to require a statement in the labeling that provides "appropriate information" regarding an off-label use if the CDRH Director states in writing: (1) there is a "reasonable likelihood" the device will be used for the off-label use; and (2) such use could cause harm. We believe this statutory authority is sufficient.
➢ *"Different Questions of Safety and Effectiveness"			
• *Inconsistent terminology*: Change "new technological characteristics" and "new types of safety or effectiveness questions to "different	"[I]nconsistency between the language in the statute and the language in the 510(k) flowchart with respect to 'technological characteristics. . . . make it challenging to consistently	FDA's changing "new technological characteristics" and "new types of safety or effectiveness question" to "different technological characteristics" and "different	FDA's longstanding interpretation of the terms "different technological characteristics" and "different questions of safety or effectiveness" with respect to the SE provisions of

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technological characteristics" and "different questions of safety or effectiveness" in the "Mohan Memorandum" to make the terminology consistent with the FDC Act and FDA's regulations.	apply the statutory review standard to determine when "different technological characteristics" raise "different questions of safety and effectiveness."	questions of safety or effectiveness" in the Mohan Memorandum, suggests that the Agency is changing the standard it uses to evaluate those key aspects of a substantial equivalence determination, even though the stated reason for the change is consistency. We are concerned that these changes would make it harder to demonstrate substantial equivalence.	the FDC Act and its implementing regulations has been that they are "new technological characteristics" and "new types of questions of safety or effectiveness questions", respectively. FDA should not change its longstanding interpretation of those terms. If the Agency makes the recommended terminology changes in the Mohan Memorandum, the Agency should define "different technological characteristics" to mean "new technological characteristics" and "different questions of safety or effectiveness" to mean "new types of safety or effectiveness questions" to preserve the Agency's longstanding interpretations of those terms. In addition, FDA should explicitly state that the new device must be compared to all of its predicate devices collectively and not each predicate device individually in order to ensure that FDA continues to use the Agency's longstanding method of evaluating those elements of a substantial equivalent determination.
• *Insufficient Guidance for 510(k) staff and industry*: Provide guidance and training for reviewers, managers, and industry to clarify how to identify "different questions of safety and effectiveness" and "different technological characteristics."	Existing guidance is unclear regarding the consideration of technological characteristics and questions of safety and effectiveness, leading to inconsistency in CDRH decisions which "can have a significant public health impact." Also, the guidance does not reflect the complex technologies of modern devices.	Guidance on the meaning of "different technological characteristics" and "different questions of safety or effectiveness" would help FDA reviewers compare a new device to its predicate device(s).	We support FDA's issuing new or additional guidance regarding the terminology used to evaluate whether a device is SE with the caveat expressed above about defining different to mean that the technological characteristic is new or that it raises new questions of safety or effectiveness. We believe any such training should focus reviewers' attention on identifying significant

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			safety or effectiveness issues and not those that would be considered theoretical possibilities, but have little or no likelihood of ever being a problem.
Assure comparison to a predicate is valid and well-reasoned, through guidance and regulation.	"CDRH's current practice allows for the use of some types of predicates that may not be appropriate."		
➢ Concerns About Predicate Quality			
• Develop "guidance on when a device should no longer be available for use as a predicate because of safety and/or effectiveness concerns."	Concerns include the use of predicates that are older, poorly-performing, recalled, no longer on the market, or for which there are several predicates between the new device and the original device that FDA cleared based on evidence of its safety or effectiveness.	FDA has indicated that the age of a device would not be the sole factor in making it ineligible to be a predicate, but the Agency has not identified the criteria it will use to determine if the device is obsolete, unsafe, or ineffective. In any case, the guidance would limit the pool of acceptable predicate devices. In addition, FDA seems to be considering requiring the manufacturer to compare its device to the original device rather than the newer device which would mean that the manufacturer would have to re-establish the relative safety and effectiveness of uses and technological characteristics that FDA has already cleared in the newer devices. This approach would hinder innovation. We cannot evaluate the full impact of the proposed guidance until FDA issues a draft of it.	FDA currently has authority to remove unsafe or ineffective products from the market. No further changes are necessary. We are concerned that lowering the standards for declaring a device to be an unacceptable predicate will result in an unnecessary reduction in the number of predicate devices.
➢ Rescission Authority			
• Issue "a regulation to define the scope, grounds, and	It is unclear to both CDRH staff and industry under what circumstances FDA could and would rescind 510(k)	FDA's rescission of a 510(k) notice means the device that is the subject of that 510(k) must be removed from the	The 510(k) Report acknowledges that the FDC Act does not explicitly authorize FDA to rescind or modify a

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appropriate procedures, including notice and an opportunity for a hearing, for the exercise of [CDRH's] authority to fully or partially rescind a 510(k) clearance."	clearance.	market or not introduced or reintroduced until it obtains new 510(k) clearance. The rescission of a 510(k) clearance could potentially call into question the clearances—and thus the continued availability—of any cleared device that used the device with a rescinded clearance as its predicate.	device's clearance. However, it states that "agencies have inherent authority to reconsider their decision in certain circumstances, such as where there has been fraud or error, and to rectify their mistake" (citations omitted) and cites two cases to support that statement. Despite that assertion, we do not believe FDA has statutory authority to rescind a 510(k) notice. If the FDA wants to rescind 510(k) notices, it must obtain the statutory authority to do so.
➢ Use of "Split Predicates" and "Multiple Predicates"			
• Disallow "split predicates," which FDA defines as "a situation in which a 510(k) submitter is attempting to "split" the 510(k) decision-making process by demonstrating that the new device has the same 'intended use' as one predicate and the same 'technological characteristics' as another." • Develop guidance and training for reviewers and managers on the use of "multiple predicates." • Provide guidance and training to "clarify the distinction between multi-parameter or multiplex devices and bundled submissions."	FDA treats split predicates inconsistently. Also, data shows that 510(k)s relying on more than one predicate have longer review times and "may be associated with more adverse event reports, on average, than 510(k)s that cite only one."	These changes would unnecessarily limit the ability to clear devices through the 510(k) process by restricting the use of predicates.	We oppose the disallowance of split predicate devices, especially since FDA is proposing to redefine intended use to include some elements of a device's indications. We request that FDA continue to allow the use of multiple predicates without any restrictions. We refrain from commenting on the establishment of longer review periods for multi-parameter and/or mulitplex devices until FDA provides data to support that action and identifies the proposed review period.

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• "[A]ssess the impact of submissions for multi-parameter or multiplex devices and bundled submissions on review times." • Establish performance goals that "account for the additional complexity of [multi-parameter and multiplex] submissions." • Analyze the connection between multiple (>5) predicates and increased adverse events.			
Reform de novo classification process "to provide a practical, risk-based option that affords an appropriate level of review and regulatory control for eligible devices."	The de novo classification process "is inefficient and has not been utilized optimally across the Center."		
• Revise the guidance to streamline the de novo classification process "and clarify [CDRH's] evidentiary expectations." • Instead of a full 510(k) review to determine eligibility for de novo classification, encourage discussion between submitters and reviewers before submission, so as to determine what information should be submitted. • Establish baseline special controls "for devices classified into class II through the de	The de novo process is impractical for many submitters because of the long time it takes to pursue both the lengthy de novo classification process and subsequently, the 510(k) processes.	The proposed changes to the de novo review process should help make the review of lower risk novel devices more efficient and consistent.	We support improving the de novo review process, including making the determination that the device is eligible for de novo review at the pre-IDE stage rather than requiring the device to be found NSE through the 510(k) process, as FDA indicated the Agency is considering doing during the September 2010 webcast about the 510(k) Report. We cannot comment on the establishment of baseline special controls for de novo devices until FDA proposes those controls.

The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
novo process, and which could be augmented with additional device-specific special controls as needed."			
Well-Informed Decision Making			
"[F]acilitate efficient submission of high-quality 510(k) device information," through guidance and regulation.	"It 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."		
➢ Unreported Device Modifications			
• Revise the guidance document "*Deciding When to Submit a 510(k) for a Change to an Existing Device*" ("the Device Modifications Guidance") to clarify which modifications to 510(k) devices require a new 510(k), a Special 510(k) or neither. • Explore whether it is feasible to require regular, periodic updates listing modifications to 510(k) devices with explanations of why a new 510(k) was not filed. • Slowly phase in the period updates, beginning with "class IIb" devices (described below).	There are concerns that manufacturers believe that new 510(k)s are only required when a modification definitively or negatively affects safety or effectiveness. Additionally, manufacturers may make a series of minor changes that cumulatively affect safety and effectiveness. When 510(k)s are not filed for modifications, CDRH lacks necessary safety and effectiveness information.	A revised Device Modifications Guidance might require 510(k) clearance for more types of device modifications. A periodic reporting requirement would mean the manufacturers must inform FDA of any modifications made in the past year, including changes for which it did not obtain 510(k) clearance and thus, the Agency would review them retrospectively. We believe that, in general, FDA's system for regulating incremental changes made between 510(k) notices balances the need for FDA oversight and companies' interest in quickly implementing minor modifications and thus, this retrospective review of all modifications is not necessary.	We believe it is not necessary to revise the Device Modifications Guidance to interpret the regulation regarding when modifications to a device require new 510(k) clearance. If, however, FDA does revise the guidance, the Agency should continue to require new clearance only for major changes that could significantly affect the safety or effectiveness of the device or constitute a major change in its intended use, as required by 21 C.F.R. 807.81(a)(3). We believe that annual reporting is unduly burdensome for both FDA and the industry because: (1) the Agency does not have the resources needed to review thousand of annual reports from device manufacturer and thus, these reports would not help FDA ensure the modifications that

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The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
			require 510(k) clearance obtain it; (2) FDA may review memoranda-to-file documenting decisions not to obtain new 510(k) clearance for device modifications during inspections. If FDA disagrees with the company's decision not obtain new clearance, the Agency can require the company to obtain 510(k) clearance in order to continue to market the device.
➢ Quality of Submissions			
• *Lack of clarity*: o Implement an "assurance case framework", which FDA defines as "a formal method for demonstrating the validity of a claim by providing a convincing argument together with supporting evidence", and develop guidance and training programs. o Explore requiring the inclusion of detailed photographs and schematics that do not contain proprietary information with a 510(k) submission. o Explore requiring manufacturers to keep at least one unit of a 510(k) device on hand to be	Unclear or otherwise insufficient 510(k) submissions are difficult to review, increase review times and make it difficult to "efficiently identify the critical features of a new device and the relevant points of comparison to the predicate."	• We believe that the impact of the proposed changes to improve the quality of the submissions would be as follows: • An assurance case framework would probably require more information and data to support changes. • FDA would likely require 510(k) notices to include photographs and schematics for posting on FDA's website. • If FDA requires manufactures to have a device available during the 510(k) review, they would either have to finalize the device prior to submission of the 510(k) notice or risk FDA placing the submission	We request that FDA issue a draft guidance on the use of assurance cases to demonstrate the validity a claim in order to determine how the type and amount of information FDA would require. We object to the provision of photographs and schematics of a device unless it is in publicly-available labeling for the device. If FDA intends to post such documents on its website, the manufacturer should be notified of such by FDA and given the option to remove propriety information or explain why such information cannot be removed from any photographic or schematic in the 510(k) notice. We vigorously object to any requirement to have a sample device available during the review of the 510(k) notice for the device and/or to retain a sample device if it is listed as

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available for CDRH review during either the device's 510(k) review or future reviews when the device is listed as a predicate.		on hold if the Agency requests to see the device. Depending on how long it would take to manufacturer to produce the device, a hold could significantly delay clearance or even result in a NSE determination if the sample device would not be available within 180 days of the request. • If FDA were to require a manufacturer to retain a sample device for the Agency's review if the device were a predicate for another device, the manufacturer would bear the cost of storing the device and making it available for FDA review, possibly solely for the benefit of a competitor. • In addition, if FDA requests the device the Agency might raise questions about the cleared device. Currently, companies are not required to actually manufacture a device for which they seek or obtain 510(k) clearance. The requirement to have and retain a sample might force companies to do so.	a predicate.

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• *Improper use of recognized standards*: o Provide guidance and training for reviewers and manufacturers regarding use of consensus standards. o Revise "the requirements for 'declaration of conformity' with a standard," for example, requiring testing summaries.	Some CDRH staff and submitters do not understand how to properly use standards in 510(k) submissions and the improper use of standards "may fail to provide meaningful or sufficient information about a device under review."	The provision of guidance and training regarding the use of consensus standards could make it easier to use compliance with standards to demonstrate substantial equivalence. The provision of test summaries in a declaration of conformance would undermine the purpose of these declarations which is to demonstrate conformance to a standard without having to provide the test report.	We encourage FDA to issue new guidance on the use of consensus standards and to provide additional training for FDA reviewers and manufacturers on their use. However, we object to the provision of information in a declaration demonstrating the device's conformance to a consensus standard, including the provision of a test summary, because the reason for a declaring conformance to a standard is so that FDA does not have to review the supporting documentation.
• *Incomplete information*: Revise 21 C.F.R. § 807.87 to require a list and description of "all scientific information regarding the safety and/or effectiveness of a new device known to or that should be reasonably known to the submitter."	Regulations do not state what clinical or scientific information may be necessary to support a 510(k) submission, and submissions frequently do not contain sufficient information, leading to delays in the review and clearance of submissions.	A requirement to list and describe all scientific information regarding the safety and/or effectiveness of a new device that is known or that should reasonably be known to the submitter would require the manufacturer to conduct an extensive literature search and prepare a detailed summary and analysis of all published information about the safety or effectiveness of the new device, as well as to describe any information it possess from testing, complaints, or that it acquired by other means. This requirement would significantly increase the cost and time to prepare a 510(k) notice. In addition, the manufacturer could be subject to criminal penalties if FDA concludes the company should knew or should reasonably have known information that was not included because the 510(k) notice includes a signed truthful and	We strongly oppose the provision of a summary of safety and effectiveness information in 510(k) notices for devices other than preamendments Class III devices for which FDA has not yet called for PMAs, which are already subject to this requirement.

The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
		accuracy statement. In addition, it is not clear how FDA would use this information to determine if a device is substantially equivalent.	
➢ Type and Level of Evidence Needed			
• Split class II devices into two subsets, IIa and IIb, where class IIb devices typically require submission of "clinical information, manufacturing information, or, potentially, additional evaluation in the postmarket setting" and develop associated guidance and training for reviewers and industry.	The 510(k) review process is lengthy and unpredictable, in part because submitters do not know how much information to include in submissions and some devices will require more supporting information than others.	The classification of generic types of devices as Class IIb and the issuance of guidance document identifying the minimum additional information required in 510(k) notices for Class IIb devices would help manufacturers of those generic types of devices provide the information needed to demonstrate substantial equivalence. However, it is unclear how FDA will handle 510(k) notices for modifications to a cleared Class IIb device because minor changes should not require new clinical data. FDA's proposed requirement for manufacturing information in essence would require that the device be manufactured prior to the submission of the 510(k) notice so that the manufacturing process will have been validated and verified prior to the submission. Thus, this requirement means that the manufacturer would bear the cost of these activities before knowing whether it could market the device. It would also increase the time to prepare the submission and likely extend the review time. (See below for our more detailed comments regarding premarket	This proposal creates a new device classification that is not authorized by the FDC Act. Congress must amend the FDC Act for FDA to implement this change. If and when Congress takes such action, FDA should issue a proposed rule identifying the generic types of devices by classification regulation number and product code that it intends to reclassify or classify as Class IIb and a draft guidance that sets forth their additional requirements. The guidance should address how FDA will regulate modifications to Class IIb devices. Section 513(f)(5) of the FDC Act states: The Secretary may not withhold a determination of the initial classification of a device under paragraph (1) because of a failure to comply with any provision of this Act unrelated to a substantial equivalence decision, including a finding that the facility in which the device is manufactured is not in compliance with good manufacturing requirements as set forth in regulations of the Secretary under

The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
		manufacturing requirements.) FDA seems to consider postmarket surveillance to be an additional requirement for Class IIb devices rather than a means to limit the data provided in a 510(k) notice to that necessary to make a substantial equivalence determination for its proposed indications.	section 520(f) (other than a finding that there is a substantial likelihood that the failure to comply with such regulations will potentially present a serious risk to human health) (emphasis added). This statutory provision prohibits FDA from withholding 510(k) clearance of a device because it is not manufactured in compliance with good manufacturing practices ("GMPs") /quality systems regulations ("QSRs") unless this noncompliance "will potentially present a serious risk to human health." For this reason, we believe that FDA cannot require manufacturing information in 510(k) notices or pre-clearance inspection regarding any devices unless the Agency finds the device potentially presents a serious health risk. Moreover, we believe that the statute requires FDA to determine whether a specific device, rather than all Class IIb devices or certain types of Class IIb devices meet that criterion.
• *Clinical information*: o In guidance, identify when clinical data will generally be required and describe the clinical data needed to support a 510(k). o In guidance or regulation, define "clinical data."	Increase efficiency and predictability by indicating to manufacturers when clinical data may be required, before a 510(k) is submitted.	Manufacturers would benefit from additional guidance regarding when clinical data is required.	We encourage FDA to issue device-specific guidance documents that identify the information needed, including the type and amount of clinical data, to demonstrate substantial equivalence. We also encourage FDA to define clinical data.

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• *Postmarket information*: o Explore increased use and expansion of CDRH's postmarket authorities "to require postmarket surveillance studies as a condition of clearance for certain devices" and develop appropriate guidance. o Continue FDA's efforts to implement a unique device identification (UDI) system. o Use "real-world" data regarding marketed 510(k) devices for future 510(k) submissions (pursuant to CDRH's implementation of a unique device identification (UDI) system).	At times, clinical data may be necessary to evaluate safety and effectiveness, but a large-scale, premarket clinical trial may not be feasible. Post-market data regarding safety and effectiveness over an extended time period or in a more diverse patient population may be necessary.	Postmarket surveillance studies might become an additional requirement for clearance for a broader range of devices rather than a way to limit the data provided in 510(k) notices to what is needed to demonstrate substantial equivalence for the proposed indications.	We believe that FDA already has sufficient authority to require postmarket studies under Section 522 of the FDC Act. We urge FDA to issue guidance regarding the criteria the agency will use to determine whether to require postmarket studies under that statutory provision. In addition, we believe that conditioning 510(k) clearance on postmarket surveillance studies may be beneficial in certain cases, but the need for and value of such studies will depend on the nature and circumstances associated with a particular device. For postmarket studies to be useful, FDA must dedicate the necessary resources and develop a robust process by which to monitor, review, and act promptly and appropriately on the findings from postmarket studies.
• *Manufacturing Process Information*: o Clarify, via guidance, when manufacturing process information may be necessary to support a 510(k) submission. o Clarify when CDRH can exercise the authority to withhold clearance due to a failure to comply with cGMPs in a way that presents a "substantial likelihood" of "serious risk	Manufacturing and quality testing procedures can affect safety and effectiveness and at times, failure to comply with cGMPs could present a risk to human health. Currently, CDRH staff are not sufficiently aware of their ability to request the submission of manufacturing information to support a 510(k).	If FDA were to require manufacturing information in 510(k) notices, that requirement would mean that the manufacturer would bear these costs before it knows whether it will be able to market the device. It also will increase the time to prepare and review 510(k) notices. Pre-clearance inspections would significantly delay clearance of devices. FDA's withholding clearance based on quality system regulations ("QSR") issues could significantly	We strongly oppose: (1) any requirement to provide manufacturing information in 510(k) notices; (2) any requirement for preclearance inspections; and (3) FDA having the authority to withhold clearance due to QSR issues except in the very limited situation authorized by Section 513(f) of the FDC Act, which is when the nonconformance with QSRs present a substantial likelihood of a health risk. One of the major differences between the 510(k) and PMA processes is that FDA's evaluation of the manufacturing process occurs pre-

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to human health." o Identify circumstances in which a pre-clearance inspection is necessary to demonstrate that a device will not present a health risk.		delay clearance and significantly increasing the cost of obtaining it.	approval for PMA devices and post-clearance for 510(k) devices. We believe that requiring manufacturing evaluation pre-clearance would blur the line between a PMA and 510(k) and undermine the 510(k) process. We do, however, support FDA's issuing guidance regarding the withholding of clearance when there is a substantial likelihood of a serious health risk due to non compliance with QSR under existing Section 513(f)(5) of the FDC Act, including the process for and the criteria used to make that determination.
Enhance internal and public information systems and databases.	Reviewers and submitters are hampered by limitations in CDRH's IT and knowledge management systems that make it difficult to access meaningful and supportive information.		
➢ Product Codes			
• Standardize the processes for developing and assigning product codes, through guidance, SOPs, and training for CDRH staff.	Product codes are developed and assigned inconsistently, making it difficult to conduct a search for meaningful and relevant device information.	Standardization of the process for developing and assigning product codes would increase the likelihood that the same product code or codes would be assigned to similar devices. This result would make it easier to identify potential predicates.	We support standardizing the process for developing and assigning product codes, by issuing guidance documents, preparing SOPs, conducting training, and other means to educate FDA staff on the need for, and ways to achieve, consistency.
➢ 510(k) Databases			
• *Limited tools for review staff and for outside parties*: o Develop a public database of cleared 510(k) devices that includes 510(k)	It is difficult for reviewers and managers to make substantial equivalence determinations because there is an insufficient record regarding the rationale for the clearance of predicates. Providing the	The provision of FDA-reviewed 510(k) summaries, photographs, schematics, histories of cleared 510(k) devices, and identification of the 510(k) notice for the original device containing the data or other	We support FDA's posting the following additional information in the Agency's 510(k) database: (1) FDA-reviewed 510(k) summaries; (2) the 510(k) history of cleared devices; (3) the identification of the original

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summaries, non-proprietary photographs and schematics, and "information showing how cleared 510(k)s relate to each other and identifying the premarket submission that provided the original data or validation for a particular product type." o Standardize the development of 510(k) summaries through guidance and SOPs. o "[D]evelop[] a standardized electronic template for 510(k) summaries."	information publicly increases transparency, decision-making predictability, and the ability of submitters to select an appropriate and accurate predicate.	validation to support clearance would make it easier to identify potential predicate devices and compare a new device to predicate devices. However, the posting of photographs and schematics of a company's cleared device would make it easier to reverse engineer the device even if these pictures do no contain proprietary information. The issuance of a guidance document, SOP, and/or template for 510(k) summaries would help ensure that all 510(k) summaries include at least the minimum required information. That information would make it easier to compare a new device to a predicate device.	device that contains the data or other information upon which clearance of a device that cited it as predicate relies. We encourage FDA to train reviewers on documenting their decisions and rationale for a substantial equivalence decision to improve FDA internal records. In addition, we support providing photographs and schematics of a device that contain nonproprietary information if FDA requires 510(k) submitters to provide such photographs and drawings for every device for which photographs and schematics can reasonably be provided, *e.g.*, device that consist only of software would not have to comply with this requirement. In addition, we support FDA's standardizing 510(k) summaries by issuing guidance documents, preparing SOPs, and proving a template if the Agency verifies that all 510(k) summaries posted contain at least the minimum information required. We urge FDA to seek the repeal of the 510(k) statement so that all 510(k) notices would include 510(k) summaries.
• *Lack of ready access to final device labeling*: o Explore whether to require submitters to provide copies of final device labeling by the time of or	"Featuring up-to-date, cleared device labeling in CDRH's public 510(k) database would allow prospective 510(k) submitters to more readily and more accurately compare their devices to potential predicates, and it would give medical professionals and device	FDA is correct that posting the draft or final labeling of cleared devices would make it easier to obtain information about cleared devices. FDA's clearance of the labeling would mean that the inclusion of	We support FDA posting the cleared draft and/or final labeling in the Agency's 510(k) database. We need additional information regarding the provision of updated labeling and/or redlined labeling in

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soon after clearance, and to provide periodic updates to device labeling. o If periodic label updates are adopted, post the labeling on the public 510(k) database after FDA has determined it is consistent with the device's clearance. o Consider the feasibility of requiring manufacturers to submit cleaned and redlined copies of final labeling and subsequent updates. o "[E]xplore greater use of software tools to facilitate rapid screening of labeling changes." o Phase in the labeling requirement gradually, beginning with class IIb devices, or a section of the label. o Post the cleared labeling on the public 510(k) website as "preliminary labeling," before the final labeling is screened.	users' easy access to critical device information that would support safe and effective use."	information in the posted labeling, including performance claims, would not constitute off-label promotion. FDA and the manufacturer's competitors could easily identify any deviations from the cleared labeling, especially if the manufacturer was required to supply and FDA posted a redlined copy of any update. FDA's requiring more detailed 510(k) summaries would likely make it easier for competitors to determine whether the company obtained 510(k) clearance for the changes.	order to evaluate these recommendation. Please clarify whether FDA would review the updated/redlined labeling, the Agency would make a determination whether the device required new 510(k) clearance based on the updated labeling, whether FDA would post the updated or redlined labeling on the Agency's website and if so, whether the Agency would indicate that it has not reviewed and/or cleared the labeling, if that is case. We have no objection to FDA exploring the use of software tools to identify changes to device labeling if the Agency commits to manually verify the changes before taking any enforcement action, including issuing a warning letter, based on them. However, such tools would not be necessary if companies were required to provide redlined labeling.
Continuous Quality Assurance			
Support consistent, high-quality 510(k) reviews through training, professional development and	"Variations in the expertise, experience, and training of reviewers and managers, including third-party		

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knowledge-sharing among reviewers and managers.	reviewers, may contribute to inconsistency or uncertainty in 510(k) decision making."		
➢ Reviewer Expertise and Experience			
• Enhance "recruitment, retention, training, and professional development of review staff," including "increased engagement with outside experts." • Create a "Center Science Council" with experienced reviewers and managers that will "serve as a cross-cutting oversight body that can facilitate knowledge-sharing across review branches, divisions, and offices. . . ."	Reviewer experience and expertise varies across CDRH and can impact 510(k) clearances. Improved training, professional development, and retention efforts will help enhance consistence across reviews.	FDA review staff would benefit from training regarding the 510(k) review process and the substantial equivalence criteria. In general, we believe that FDA's consultation with outside experts, especially practicing clinicians, would improve, but there needs to be a process in place for ensuring that the expert consulted is appropriate and for information to be shared with the manufacturer. Our views on the impact of the Center Science Council are provided below.	We urge FDA to recruit, retain, train, and enhance and support the professional development of Agency reviewers. FDA's consultation with outside experts other than through the panel process must be done in a transparent manner. We request that FDA issue a draft guidance document regarding the appropriate use and documentation of communications with outside experts. Our proposed comments regarding the Center Science Council are provided below.
➢ Third-Party Review			
• Regularly evaluate and revise which types of devices are eligible for third-party review. Limit eligibility for third-party review to device types which have a device-specific guidance document in place, or make ineligible certain devices with a history of design problems. • "[E]nhance [the] third-party reviewer training program."	Although third-party-reviewed submissions are cleared faster than other 510(k)s, there is a concern about the quality of third-party reviews and about the training and experience of the third-party reviewers.	FDA's recommended changes to the third-party review process would limit the types of devices eligible for third-party review. However, better training of third party reviewers and sharing more information with them should increase the quality of third-party reviews.	We support FDA's recommendations regarding third-party review if the Agency develops the proposed guidance.

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• "[S]hare more information about previous decisions with third-party reviewers . . . ."			
Support continuous quality assurance through enhanced system and program metrics.	"CDRH does not currently have an adequate mechanism to regularly assess the quality, consistency, and effectiveness of the 510(k) program."		
• Continuously assess the 510(k) program's quality, consistency and effectiveness and measure the effect of any reforms to the system. • Audit review decisions for adequacy, accuracy and consistency, as overseen by the Center Science Council (described above).	Existing review programs are not sufficient to assess the performance of the 510(k) program.	FDA's assessing and auditing the 510(k) review process probably would help the Agency identify problems. If FDA has the resources to address such problems, than this oversight would help the Agency improve the 510(k) process. However, it presents a risk that FDA will "second-guess" some of 510(k) decisions or find new information which could lead to FDA's trying to rescind cleared 510(k) notices, requesting that the submitter withdraw cleared 510(k) notices, or require the submission of new 510(k) notices unless appropriate safeguard are implemented.	We support FDA's assessment and auditing of the 510(k) process if the Agency has procedures in place for ensuring that the information is used solely to evaluate the 510(k) process and not used to reconsider individual 510(k) clearance decisions.
The FDA TASK FORCE'S NEW SCIENCE REPORT			
Enhancing CDRH's Scientific Knowledge Base			
• **Improve the ability of CDRH to readily access high-quality information about regulated products.**	It is difficult for CDRH to obtain complete information about risks and benefits of regulated products across the total product life cycle. Insufficient information limits the Center's ability to make decisions		

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	based on changes of a device's risk/benefit profile.		
➢ "Premarket Review"			
• *Least burdensome:* Revise 2002 guidance to clarify the interpretation of "*least burdensome*" provisions of the FDCA (21 U.S.C. §360(a)(3)(D)(ii) and 21 U.S.C. §360c(i)(1)(D)).	There is a need to communicate to industry that the "*least burdensome*" provisions are not intended to excuse industry from pertinent regulatory obligations nor to lower the agency's expectations about what is necessary to demonstrate that a device meets the relevant 510(k) statutory standard.	Revision of FDA's 2002. guidance document on "least burdensome" would provide an opportunity to develop a more predictable and transparent process for incorporation of new risk/benefit data into the 510(k) premarket review process. FDA should ensure that Agency staff are also trained on the least-burdensome principals so that there is consistency in the interpretation across reviewers.	We support FDA's revision of its Least Burdensome guidance to provide clarity to both manufacturers and FDA reviewers on the interpretation of those provisions.
• *Quality of Clinical Data*: Establish a team of clinical trial experts, as a subset of the proposed Center Science Council, to: o Provide support to CDRH staff regarding clinical trial design and data quality in IDE applications; and o Serve as a review board when there are differences of opinion about clinical trial design and interpretation of the proper application of the "least burdensome" principle.	The "*quality of clinical data*" recommendations are driven by concerns within and outside the Center that the quality of clinical trial design and data used in support of both PMA and 510(k) submissions is inconsistent, leading to limitations in the ability of CDRH reviewers to assess a device's risks and benefits. In addition, poor quality clinical trials can prevent approval/clearance of promising innovative devices. The rationale is to create an internal team with clinical trial expertise that will also serve as a central CDRH review board to address differences of opinion regarding clinical trial design and application of the "least burdensome" concept.	The strength of the proposal is the potential to improve expertise and consistency across CDRH regarding clinical trial design and quality of data applicable to diverse medical devices. The feasibility of implementing a clinical trail expert team and utilizing the team in a consistent and predictable manner, however, is unclear. If the team of clinical trial experts is to be used to resolve disputes, FDA must establish clear processes and policies on how to bring disputes before the clinical trial team, the criteria the team will use to resolve disputes, and any recourse or appeal process that a manufacturer might use if it disagrees with the team's opinion.	While we agree with the concept of a cross-cutting team of clinical trial experts, we urge FDA to consider whether it is feasible to create such a team and ensure consistent and predictable review by the team. Additionally, we strongly encourage FDA to issue guidance, SOPs, etc., describing how the clinical trial expert team will be utilized, what types of disputes may be brought before the team, timelines for review, etc.

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• Engage in development of U.S. and international consensus standards for clinical trial design, performance and reporting. • Expand ongoing efforts related to improvement of PMA clinical trials to include clinical trials that support 510(k)s.			
• *Quality of Clinical Data*: Characterize the root causes of challenges in IDE decision making and take steps to enhance pre-submission interactions with industry, including development of new guidance on pre-IDE submission interactions between industry and center staff.	Although disagreements about the need for clinical data is cited by CDRH as a factor that disrupts IDE decision making, additional other factors are not completely understood.	An in-depth review of the challenges in IDE decision-making process and new guidance on pre-IDE procedures and expectations could lead to more productive pre-meetings with the agency and consistency and predictability in the information needed to support premarketing submissions, including PMAs and 510(k)s.	We support this recommendation but urge FDA to consult with industry and stakeholders during the process.
• *Review workload*: Create a mechanism to rapidly assemble an experienced ad hoc team to assist with time-critical premarket review work.	Stop-gap measure is needed to resolve current workload challenges in premarket review.	This proposal has the potential to provide short term relief for the chronic problem of insufficient staffing to meet the mandated review deadlines, especially the 30-day review period for IDEs. However, to do so effectively, the ad hoc team must have the appropriate expertise. If not, this proposal could lead to fragmenting the review process and bringing in review personnel who are unfamiliar with the device's technology or intended use, which may ultimately delay the review and clearance/approval of clinical trials	We support the use of an ad hoc team to review IDEs, 510(k)s, and PMAs when necessary to meet review deadlines However, we caution FDA that the ad hoc teams could delay the review and clearance/approval of clinical studies and/or the device. especially if different teams review the IDE and the 510(k) notice or PMA.

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• Characterize the challenges in reviewing IDEs within the mandatory 30-day timeframe and develop solutions under the Center's existing authorities.	Data are provided in the report regarding the IDE review workload, staffing, and concerns about the ability of the Center to complete reviews within the 30-day timeframe.	and/or the device. An in-depth review of the challenges associated with the IDE review process and current workload issues review of review process could lead to improvement and predictability of the process.	
➢ "Postmarket Oversight"			
• Develop better methods for collecting and analyzing postmarket device safety data. This will build on CDRH active effort to establish unique device identification (UDI) system that can be incorporated into health care patient data systems. • Invite industry and other external parties to collaborate and voluntarily submit data about marketed devices.	A broad and long-term approach to postmarket oversight is needed to facilitate analysis of postmarket adverse event reporting and to allow CDRH to access "real world" large-scale electronic data systems.	FDA and other stakeholders have already identified concerns related to the detection of safety signals in "real world" databases, including the process of determining if the signal is real, what its true magnitude is, and whether the signal is actionable.	We support this proposal but caution FDA that clear procedures and processes must be in place to ensure consistency.
• **Address staffing needs and enhance processes and systems that support Center-wide integration.** • Conduct an assessment of staffing needs to accomplish mission-critical functions.	Current staffing levels, training, and knowledge management infrastructure limit Center-wide sharing of scientific knowledge and the development of new knowledge. There are too few experts within each content area, some areas with no clinical experts, and expertise may sometimes be inadequate to evaluate novel technologies.	Increasing the number of experts, including clinical experts, in some review areas will likely lead to more knowledgeable and timely premarket reviews.	We support these proposals.

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• Enhance employee training and professional development.	This is a goal, supported by data, already identified under FY 2010 Strategic Priorities to enhance recruitment, retention, and development of high-quality employees.	Improvement in employee training and professional development may enhance the review process and lead to better retention of experienced reviewers.	
• **Improve mechanisms for leveraging external scientific expertise.**	It is difficult for CDRH to tap meaningful external scientific expertise in a timely manner.		
• Develop a web-based network of external experts.	There a need for CDRH to access information about novel technologies, new scientific issues, and improve internal scientific capabilities. The intent is to increase the use of outside experts via web-based mechanisms distinct from the regulated process of formally accessing outside experts via the Advisory Committee and other Special Government Employee mechanisms.	The strength of this proposal is that increased access to outside experts has the potential to enhance the growth of scientific expertise within CDRH. However, it is possible that the use of external experts could have decisive influence on premarket and postmarket regulatory decisions affecting single products or groups of devices. The establishment and use of any external experts should be done in a manner that assures that the identity, opinion, and potential bias of the "external expert" will be transparent to the manufacturer and the public during the review process.	We urge FDA to publish its draft standard process for the establishment and utilization of the proposed web-based network of outside panels. We reserve our comments until that proposals is published.
• Develop standard processes for use of external experts.			
• Establish enduring collaborative relationships with other science-led organizations.	Mechanism for additional access to external scientific expertise.	CDRH already interacts with professional medical and scientific associations. Establishing long-term collaborations with such experts would FDA gain insight into issues that it might not otherwise have fully considered.	We support this proposal.

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Applying a Predictable Approach to Determine the Appropriate Response to New Science			
• **Establish an approach, as predictable as practical, for determining what action is warranted in response to new scientific information that could affect regulatory decisions about devices. The conceptual framework is a four-step approach. of detection, escalation, collaborative deliberation, and action.**	Across the Center, it is not clear when new scientific information warrants action by CDRH, particularly a change in evidentiary expectations for premarket review of a product or group of products.	The conceptual four-step approach proposed by FDA would greatly improve appropriate evaluation and response to new information related to a device or group of devices. However, the implementation of such a framework and the consistency of how it is applied is of great concern. The current proposal lacks important detail and definitions, such as identification of a "signal", when it should be escalated, etc.	We support the recommended conceptual framework. However, we have serious concerns about the feasibility of implementing and utilizing such a framework in a timely and consistent manner. We encourage FDA to provide greater detail, through the development of standard procedures, guidance, etc., on the implementation of the proposed framework and to invite comments from industry and stakeholders on those processes.
• Develop and implement a process of "**Signal Escalation**" of new science signals, including detection, escalation to upper management, process for deliberation, and decision for action. Also, develop metrics to determine if the new process is effective.	CDRH lacks a process that is followed by *all* review divisions to determine if new information warrants a change in evidentiary requirements for devices that are reviewed. The rationale for proposal is to ensure consistency in management of new science signals that could affect 510(k) regulatory decisions, assure open internal communication, and develop a collaborative response, as well as to, avoid duplication of effort.		CDRH is already developing a Signal Escalation process. We strongly encourage FDA to obtain stakeholder feedback on the process and to develop procedures for revising the process if the metrics show the process is not effective.
• Develop a **Collaborative Deliberation** process to determine what action, if any, is necessary in response to new scientific information. This includes establishment of a Center Science Council within CDRH, under	CDRH lacks a central authoritative team with experience and expertise - including clinical trial expertise - needed to interpret whether new requires new regulatory action.	Again, we agree with the concept of a Collaborative Deliberation process, but are concerned with the practical implementation of such a process. The development of a Center Science Council could have a profound effect on the regulation of single products or groups of devices. In addition, the Center Science Council is to serve as	We support the recommended conceptual framework. However, we have serious concerns about the feasibility of implementing and utilizing such a framework in a timely and consistent manner. We encourage FDA to provide greater detail, through the development of standard procedures, guidance, etc.,

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direction of the Deputy Center Director for Science, to provide oversight and consistency in responding to new science information.		a review board to resolve certain disputes; thus, this may mitigate internal disagreements that have focused negative media and Congressional attention on CDRH. However, the use of the Center Science Counsel could lead to delays in premarket review and evaluation of new science unless FDA issues detailed procedures for its establishment and utilization.	on the implementation of the proposed framework and to invite comments from industry and stakeholders on those processes.
• Enhance data sources and methodologic capabilities for evidence synthesis and decision-making as a long-term goal.	There is a need to improve the infrastructure for quantitative science-based decision-making for device regulation because CDRH operates in environment of rapidly changing technology and science.	Improvement in data capture, methods, and analysis is a major goal for both FDA and industry regarding regulated devices. However, stakeholders have already identified concerns related to the use of real world clinical databases for low-frequency safety signal detection, including the process of determining if the signal is real, what its true magnitude is, and whether the signal is actionable (e.g., FDA's ongoing development of the Sentinnel Database).	We support this proposal and urge FDA to develop clear definitions, processes, and procedures to ensure consistency.
Promptly Communicating Current or Evolving Thinking to All Affected Parties			
• **Make use of rapid communication tools to convey changes in the Center's thinking and expectations.**	In response to new science that affects regulatory decision-making, it is difficult for the Center to communicate current or evolving thinking in a timely and meaningful manner to all stakeholders.		
• Streamline processes for developing guidance	There is need for more rapid capability to implement changes in FDA policy	More streamlined and timely delivery of needed guidance and correction of	We support this recommendation.

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documents and regulation, consistent with FY 2010 Strategic Priorities. Also, encourage industry and other parties to submit proposed guidance documents.	at the levels of guidance and rule making, particularly to address a public health concern or lessen burden on industry.	ambiguous regulations may increase predictability in the PMA and 510(k) review process. However, there must be sufficient opportunity for public comment and discussion. Additionally, the ability to actually achieve this goal may be difficult given the current limitations of CDRH staffing and resources.	
• Establish a standard practice of issuing open "**Notice to Industry**" letters to all manufacturers of a group of devices when CDRH has changed its regulatory expectations in response to new scientific data.	The Center currently lacks the ability to rapidly and consistently disseminate evolving regulatory expectations for a general type of devices. The proposed Notice to Industry letters would in effect be considered guidance and would be issued as Level 1 guidance documents. CDRH would open a public docket for submission of comments upon issuance of Notice to Industry letters and follow with more specific, detailed guidance describing the new information and changes in expectations.	The notion of clear written communication of major changes in FDA expectations has the potential to create a "level playing field" for all manufacturers when FDA changes its thinking about a group of products. However, implementation as a standard practice *prior to the opportunity for public comment and feedback from industry* may have the unintended consequence of increasing the frequency of abrupt changes in regulatory expectations for many groups of devices without appropriate input from manufacturers or the public. There is the possibility that FDA could further revise its expectations for premarket submissions for a group of devices based on comments the Agency receives after it issues the Notice to Industry letter and subsequent detailed guidance. This could create an even more "unlevel" playing field for manufacturers because some would have been required to comply with the expectations outlined in the Notice to Industry letter while others would only need to comply with the	We support the internal committee's proposal for early and frequent communication regarding new science and evolving expectations. However, we caution FDA about the potential unintended consequences of Notice to Industry letters and recommend that such letters be used to invite industry to meet with the Agency.

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		revised expectations issued in the final guidance.	
• Create a web page to identify and explain the new science information that has changed the Center's regulatory expectations.	There is a need to promote better public understanding of rationale for changes in the Center's regulatory requirements across all CDRH-regulated products.	If FDA does implement the new process of issuing "Notice to Industry," an explanatory web page would provide an accurate account of FDA's thinking and provide industry with an opportunity to evaluate FDA's rationale in the context of its own specific device. The explanatory web page, however, should not identify specific devices or companies, but present information in aggregate and general format.	We support an explanatory website, if the new Notice to Industry letter process is implemented.
• Develop online access to up-to-date labeling for 510(k) devices.	"Featuring up-to-date, cleared device labeling in CDRH's public 510(k) database would allow prospective 510(k) submitters to more readily and more accurately compare their devices to potential predicates, and it would give medical professionals and device users' easy access to critical device information that would support safe and effective use."	Our views on the potential impact of the review and posting of 510(k) cleared labeling on FDA's website are discussed above in the 510(k) Report section of this table.	Our comments on the review and posting of 510(k) cleared labeling on FDA's website are discussed above in the 510(k) Report section of this table.
• **Provide additional publicly accessible information about the Center's response to new science and reasons for its actions.**	There is a lack of transparency about the rationale for particular courses of action by CDRH in response to new scientific data applicable to individual devices and groups of medical devices.		We support the higher level concept of provision of publicly accessible information about the Center's rationale for decision-making.
• Develop a publicly accessible SOP that describes the process CDRH will use to respond to new science, including "Signal Escalation" described	There is a need for clear and prompt communication in a standardized manner of new CDRH regulatory decisions and their rationale, particularly when the decision is a change in evidentiary expectations for clearance of a particular type of	It is critical that FDA define the process and criteria that it will use during "Signal Escalation," Collaborative Deliberation, and Action/Communication to publicly or not publicly communicate a change in regulatory expectations for a device	We reserve comment on the process for FDA's responding to new science until the Agency publishes the proposed SOP.

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The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
above.	product.	or group of devices. It is also critical that the process define the formal mechanisms for informing a manufacturer that "Signal Escalation" has been initiated, ensuring input of the manufacturer, and defining a process for dispute resolution.	
• Make sure all CDRH staff understand what information they are permitted to discuss with manufacturers.	Many manufacturers perceive that there is inconsistency and confusion across review teams as to what information may be communicated to the Sponsor regarding the rationale for a substantial equivalence determination. Additionally, training for CDRH staff could avoid needlessly withholding information that would clarify the basis of a particular action/decision.		We support training FDA staff regarding the type of information that can be shared, but urge the Agency to ensure that its staff fully explains the substantial equivalence determination to the submitter while ensuring that proprietary information regarding the predicate devices is not shared with other companies.
• Continue to make more premarket and postmarket information about CDRH regulated products publicly accessible thought the CDRH Transparency Website.	This recommendation is consistent with the Center's FY 2010 Strategic Priorities and the efforts of the FDA Transparency Task Force.	Continued use and improvement of the CDRH transparency website can provide industry and the public with more information about medical devices and CDRH's decision making process. However, there must be mechanisms in place to assure that confidential information will remain confidential. In addition, FDA must develop and implement policies and procedures regarding type of information the Agency will publicly disclose and timing of such disclosure.	We support this recommendation, but remind FDA that the public disclosure of information must comply with the current regulations regarding confidential, trade secret commercial information set forth in 21 C.F.R Part 20.
• Publicly release information that is currently not available, including summaries of premarket review		Posting of premarket decision summaries may increase the consistency of the review process and allow manufacturers to choose more appropriate devices as predicates or	We support this recommendation.

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The FDA Internal Committees' Recommendations	The FDA Internal Committees' Stated Rationales for Their Recommendations	King & Spalding's Views on Potential Impact of the Recommendations, if Implemented	King & Spalding's Comments on the Recommendations
decisions as well as the results of agreed upon post-approval studies and required postmarket Section 522 studies.		controls in a clinical study.	

October 4, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Comments of the Patient, Consumer, and Public Health Care Coalition

on

"Center for Devices and Radiological Health Preliminary Internal Evaluations"

[Docket No. FDA-2010-N-0348]

As members of the Patient, Consumer, and Public Health Coalition, we support most but not all of the preliminary recommendations of the 510(k) Working Group and the Task Force on the Utilization of Science in Regulatory Decision Making.

We do not support the recommendations regarding the de novo process or third party review. We also want to express our concerns about the Class IIb category and the off-label use recommendations.

We agree with the Working Group's finding that "CDRH does not currently have an adequate mechanism to regularly assess the quality, consistency and effectiveness of the 510(k) program."[1] That is consistent with what members of our Coalition have said in our March 19 public comment and at the FDA's "Strengthening the Center for Devices and Radiological Health's 510(k) Review Process" meeting in February.

The scope of this finding is broad and cuts to the heart of the problem with the 510(k) program. The 510(k) program clears devices based on similarity to predicate devices. But if a new 510(k) device is based on a predicate that had poor quality, safety issues, or was ineffective, how can we expect the new device to be any better? And if the new device is made of different materials or uses a different mechanism of action, it is impossible for the FDA (or doctors or patients) to be certain that the new product is as safe or as effective as the predicate.

Below are our comments on several of the Working Group's specific recommendations.

Substantial Equivalence

We agree with the Working Group that CDRH should clarify the meaning of substantial equivalence through guidance and training. Substantial equivalence must be consistently

interpreted by CDRH, and the interpretation should be tightened to safeguard the public health.

We also agree that the FDA should clarify what it means that the product should have the same intended use. We agree that the interpretation has been flexible to the degree that it is unpredictable. We were very concerned that the CDRH's own survey found confusion among reviewers, many of whom did not realize "that a device with a new "intended use" cannot be found substantially equivalent."[1] Moreover, we strongly urge the FDA to use established public health and scientific standards to determine if a product is substantially equivalent and whether different technological characteristics raise different questions of safety and effectiveness.

In the past, the focus of the 510(k) process has been on letting companies change devices in the name of innovation, not based on public health standards. As a result of this focus on innovation, devices are being cleared as "substantially equivalent" that are in fact substantially different from previous devices. In the absence of clinical trials, it is often not possible to determine exactly what the risks and benefits are likely to be, and it is certainly possible that the newly cleared device is not be as safe or effective as other products on the market. This lack of more stringent criteria for clearance and lack of information about safety and effectiveness potentially costs the medical system (and individuals) billions of dollars each year. Patients may buy or use products that don't work as well as other available products, or they spend a great deal of money to treat health problems that result from the complications of devices that are not as safe as other available products.

Predicate Devices

The 510(k) process has been based on the assumption that a medical device that is "substantially equivalent" to one already on the market does not need clinical trials to determine its safety or efficacy. The definition of substantially equivalent is loosely defined. In 2009, the FDA admitted that "Our Review identified multiple sources of disagreement and confusion about 510(k) standards and practices, including the standards in the FDC Act and FDA's regulations."[2] We strongly urge that the definition be tightened to ensure to better ensure the new products' safety and efficacy.

We agree with the Working Group's assessment of split predicates. The Working Group stated, "The use of a 'split predicate' is akin to combining different attributes of more than one device into a single, nonexistent predicate device, whose risks and benefits are unknown." The group further stated that CDRH should "explore the possibility of explicitly disallowing the use of 'split predicates.'"**Error! Bookmark not defined.** We agree.

We strongly support the Working Group's recommendation that CDRH conduct additional analyses to determine why 510(k) applications that cite more than five predicates are more likely to have a substantially higher rate of adverse event reports.

While this review is underway, the FDA should not allow applicants to cite more than five predicates.

We agree with the Working Group that predicates that are no longer considered safe or effective or that would represent substandard care should not be sufficient for a 510(k) review. The most extreme example is when devices that have been withdrawn from the market due to safety or effectiveness issues are used as predicate devices. This practice clearly put patients' safety at risk and should be prohibited. Moreover, if the new device application is intended to be reviewed as substantially equivalent to a device that is still on the market, if its predicate was withdrawn because of safety or effectiveness, subsequent devices should not be available as predicates. This is necessary because there is often a delay between when a product is cleared and when safety or effectiveness issues become apparent.

However, even if the predicate is not recalled or withdrawn, it may still be substandard because of newer devices or treatments that are available, and in that case should not be considered an adequate predicate.

The Working Group stated that guidance regarding when a device should no longer be used as a predicate should be "well-reasoned, well-supported, and…unintended consequences should be carefully considered." The term "unintended consequences" has been used by industry in the past as an argument against strict standards. They argue that an unintended consequence of strong safety regulations is that it will restrict innovation. However, the unintended consequences of some devices have included injuries and deaths. Those safety issues should be CDRH's main concern.

We support the Task Force's recommendation that CDRH should clearly communicate to industry that the "least burdensome" guidance is not intended "to lower the agency's expectations"[3] on what is necessary to meet statutory standards.

Off-Label Use

We find the Working Group's recommendation regarding off label use to be too vague. It recommends considering a statutory amendment to the FDCA "that would provide the agency with the express authority to consider an off-label use, in certain limited circumstances…Such circumstances would include the availability of compelling evidence that the primary use of the marketed device will be off-label."[1] If CDRH has reason to believe that a primary use is expected to be off-label, then CDRH should insist that the application for clearance or approval be revised to provide scientific evidence that the device is safe and effective for that likely use. That assessment should be strongly influenced by the public health implications, and should influence the FDA analysis of whether the device is high risk, and whether it requires a PMA.

Rescission Authority

The FDA does not have clear authority to rescind clearance once a 510(k) device is cleared. According to FDA's Director of the Office of Device Evaluation, "it is difficult to fix/modify or remove a cleared 510(k)."[4] Rescission authority is essential since these devices are often cleared with little or no data from clinical trials. Rescission authority is especially urgent for devices that were cleared prior to the newly proposed improvements to the 510(k) process.

We support the Working Group's recommendation to issue a regulation defining when CDRH can fully or partially rescind a 510(k) clearance. For example, if new data emerges once a device is on the market that shows the device may be unsafe or ineffective, then CDRH should be able to act on that scientific evidence and rescind the 510(k) clearance. It would be foolish to ignore postmarket data or to tie CDRH's hands and not allow CDRH to act on those data.

The De Novo Classification

The de novo process is intended for lower risk devices that do not have a predicate device. We have strong concerns about the Working Group recommendation that the de novo process should be streamlined and that CDRH should "assure that it is utilized appropriately across the Center."**Error! Bookmark not defined.** In our opinion, the de novo process is a short-cut for devices that should be proven safe and effective through the Premarket Authorization (PMA) process.

Class IIb Devices

We are very concerned about the proposed Class IIb category. Although we favor more stringent review of 510(k) cleared devices, we opposed the Working Group statement that "potential candidates for this device subset may include implantable devices, life-sustaining devices and life-supporting devices." All implantable, life-sustaining, or life-supporting devices should be reviewed through the PMA process. Although there are implantable devices that are not life-sustaining or life-supporting, the failure of an implanted device is often a high-risk event. That is why the law requires that high risk devices be approved through the PMA process. It would be a disaster to lower that standard.

In fiscal year 2010, the FDA charged a standard fee of only $4,007 for a 510(k) submission (and only half that amount for small companies) and $217,787 for an original PMA (one-quarter that amount for small companies)[5] Both are well below the actual cost to the FDA of doing reviews. Since the PMA user fees are hundreds of thousands of dollars below the actual cost of a thorough PMA review, CDRH will continue to lack the resources needed to use the PMA process as often as it should. In addition, the much lower user fees, shorter time-lines, and drastically smaller expense for the company submitting a 510(k) application provide an enormous incentive for companies to pressure the FDA to review their products through the 510(k) process.

There are Class II devices that could benefit from a higher standard of review, such as contact lenses and contact lens solutions, since either can cause blindness or debilitating damage to vision. However, life-sustaining, life-supporting, and implantable devices should be Class III devices and reviewed through the PMA process.

A recent study by the National Research Center for Women & Families found that for the last ten years, the vast majority (nearly 80%) of what FDA considers Class I Recalls—defined as devices recalled because they can cause serious harm or deaths—were 510(k) cleared devices. These recalls have involved millions of devices that were taken off the market, jeopardizing the health of millions of Americans. Class IIb has the potential to dramatically increase those risks. If devices can cause serious harm when they fail such, as implanted devices or devices used to diagnose cancer or other serious diseases, they should not be cleared through the 510(k) process.

Post Market Surveillance

We agree with CDRH's statement that postmarket tools "have important limitations and are not sufficient to serve as a substitute for high-quality premarket review."**Error! Bookmark not defined.**

We agree with the recommendation that CDRH explore greater use of its postmarket authorities" and "seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices," as we mentioned in the Rescission Authority section. We also agree with the recommendation that CDRH "implement a unique device identification (UDI) system" and use real world data (anonymous data) as part of a premarket submission for future 510(k)s.

Manufacturing Process Information

We agree that CDRH should clarify when it will withhold clearance on the basis of a failure to comply with good manufacturing requirements. If device makers do not comply with good manufacturing requirements, then their devices should not receive clearance, regardless of whether it is Class I, Class II, or Class III.

Although the FDA states that the "majority of recalls are due to manufacturing and design control problems,"[6] the FDA does not inspect the manufacturing plants of 510(k) products prior to clearance. The agency therefore misses an opportunity to spot contamination, manufacturing flaws, and changes in device design or materials. In addition, key manufacturing information such as engineering specifications about the device design and assurances of on-going quality, may not be included in the 510(k) review process.[7] In contrast, the GAO points out that the agency does inspect manufacturing establishments as part of its review of original PMA submission.[8]

Informed Decision Making

CDRH should provide device makers with clear instructions about its evidentiary expectations. This helps industry by making the process more fair and predictable. In

turn, device makers have an obligation to provide CDRH with all pertinent data about their devices, not just the studies that show the benefits of the device. We support the Working Group's recommendation that CDRH explore the feasibility of requiring manufacturers to provide regular, periodic updates to the Center listing any changes to its devices and if those changes do not require a new 510(k), then clearly explain why the changed device does not need a new 510(k). In fact, we believe that CDRH should ensure that those updates are feasible.

We support the Working Group's recommendation to revise regulations "to explicitly require 510(k) submitters to provide a list and brief description of all scientific information regarding the safety and/or effectiveness of a new device known to or that should be reasonably known to the submitter."**Error! Bookmark not defined.**

Under quality of submission, the Working Group recommended that a new "guidance should also clearly reiterate the long-standing expectation that 510(k)s should describe any modifications made to a device since its previous clearance."**Error! Bookmark not defined.** If necessary, Congress should consider a change in statute to ensure that.

Third-Party Review

We do not support third-party reviews. CDRH should do all the reviews. The FDA has expressed concerns about the poor quality of third party 510(k) reviews, stating that "most 3rd-party-eligible devices do not have a device-specific guidance [and] accredited parties do not have access to previous decisions/reviews of the device type."[7]

Third-party reviewers have an innate conflict-of-interest. If a device manufacturer considers a third-party reviewer to be too strict, the manufacturer will shop around for a reviewer who is less stringent in the future. Third-party reviewers know this and that provides them with an incentive to not be as strict as they should be. A review process that depends on the company whose product is being reviewed hiring the reviewers is by definition flawed and subject to unacceptable conflicts of interest.

Information Technology

We support the Working Group's recommendations to improve CDRH's 510(k) databases so that they provide more complete and up-to-date device information. All of this information should be publicly available in an easily searchable database that includes a verified 510(k) summary. CDRH should develop a standardized electronic template for 510(k) summaries, which will help to make the database more accurate and complete.

Tools for Quality Assurance

We support the Working Group's recommendation for a new Center Science Council to continuously monitor the 510(k) program's performance and effectiveness, and facilitate knowledge-sharing across review branches to improve internal communication.

Comments on Volume II – Task Force on the Utilization of Science in Regulatory Decision Making (Preliminary Report and Recommendations)

We agree with the Task Force's recommendation that "CDRH take proactive steps to improve the quality of premarket data, particularly clinical data…and develop better data sources, methods, and tools for collecting and analyzing meaningful postmarket information."[3]

We are concerned about the recommendation "to improve knowledge management…by developing a web based network of external experts, using social media technology."[3] How will CDRH ensure the objectivity and lack of conflicts of interest of the external experts? The Task Force stated that CDRH needs to "develop standard business process for the appropriate use of external experts to assure consistency and address issues of potential bias"[3] but it is not clear that will be possible, especially given CDRH's limited resources.

We support the Task Force's recommendation that CDRH establish a Center Science Council with experienced employees and managers from CDRH "to help assure consistency across the Center in responding to new scientific information."[3] However, procedures must be put in place to avoid one person or a few people from dominating the process. Perhaps staff should serve on a rotating basis.

We strongly agree with the Task Force's recommendation that "CDRH continue its ongoing efforts to improve the quality of the design and performance of clinical trials used to support premarket approval applications (PMAs)."[3] Currently, the standards for clinical trials of devices are inferior to the standards for prescription drugs in terms of number of studies, sample sizes, and methodologies used. We also strongly agree with the recommendation that CDRH expand its efforts "to include clinical trials that support 510(k)s."[3] Too many devices are cleared for the market without solid evidence from clinical trials that the devices are safe or effective.

We agree with the Task Force's postmarket oversight recommendations and that CDRH should conduct a data gap analysis.

Regarding the Task Force's recommendation to streamline its guidance documents process, we support CDRH using the "Level I—Immediately in Effect" option for guidance "intended to address a public health concern."[3] However, we do not support this for lessening the burden on industry, as the Task Force recommends.

We support the Task Force's common-sense recommendation that CDRH develop Standard Operating Procedures in order to respond to new scientific information.

We support the Task Force's recommendations on transparency. We strongly support the recommendation "to release summaries of premarket review decisions to the CDRH Transparency Website."[3]

Summary

As members of the Patient, Consumer, and Public Health Coalition we support most of the recommendations regarding 510(k) improvements but do not support the recommendations regarding third party review or the de novo process. We have also expressed our concerns about the proposed Class IIB category and off-label considerations. Overall, our most important feedback is to urge the CDRH to ensure that changes greatly strengthen existing safeguards to protect the public from products with questionable benefits or unproven safety. We believe that doing so will benefit device manufacturers as well as patients and consumers. We urge CDRH to consider our comments as it works to better fulfill its mission of protecting and promoting the public health.

Breast Cancer Action
Center For Medical Consumers
Community Access National Network (CANN)
Government Accountability Project (GAP)
National Research Center for Women & Families/Cancer Prevention and Treatment Fund
National Women's Health Network
Our Bodies Ourselves
Reproductive Health Technologies Project
The Scientific Integrity Program, Union of Concerned Scientists
THE TMJ Association
Truth in Medicine
WoodyMatters

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[1] Food and Drug Administration (August 2010). CDRH Preliminary Internal Evaluations—Volume I, 510(k) Working Group, Preliminary Report and Recommendations.

[2] Food and Drug Administration (2009). Review of the ReGen Menaflex®: Departures From Processes, Procedures, and Practices Leave the Basis for a Review Decision in Question.

[3] Food and Drug Administration, Center for Devices and Radiological Health (August 2010). CDRH Preliminary Internal Evaluations—Volume II, Task Force on the Utilization of Science in Regulatory Decision Making, Preliminary Report and Recommendations.

[4] Food and Drug Administration, Center for Devices and Radiological Health. (March 2010). Understanding the Premarket Notification (510(k)) Process. FDA's 510(k) Working Group. Presentation to the Institute of Medicine by Donna-Bea Tillman, Ph.D., Director, Office of Device Evaluation.

[5] [4]Department of Health and Human Services, Food and Drug Administration, Federal Register Notice [Docket No. FDA-2009-N-0338] (August 2009). Medical Device User Fee Rates for Fiscal Year 2010. US Government Printing Office Web site.

[6] Food and Drug Administration (February 2010). FDA's 510(k) Workshop: Issues Related to New Technologies and Scientific Evidence presentation by Arleen Pinkos, Scientific Revie3wer, Office of In Vitro Diagnostic Device Evaluation and Safety, CDRH.

[7] Food and Drug Administration (February 2010). FDA's 510(k) Workshop: Issues Related to the Following Types of Submissions: Bundled, 3rd Party, and Submissions which Contain Standards presentation by Barbara Zimmerman, Deputy Director for Premarket Program Management, Office of Device Evaluation, CDRH.

[8] Government Accountability Office (January 2009). Medical Devices: FDA Should Take Steps to Ensure that High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process.

America's Health Insurance Plans

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October 4, 2010

Leslie Kux
Acting Assistant Commissioner for Policy
Division of Dockets Management (HFA-305)
Food and Drug Administration,
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Dear Ms. Kux,
Thank you for the opportunity to comment on the Food and Drug Administration's (FDA's) Federal Register notice and request for public comments on the two preliminary internal evaluations, *Volume I: 510(k) Working Group Preliminary Report and Recommendations & Volume II: Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations.* America's Health Insurance Plans (AHIP), the national association representing nearly 1,300 health insurance plans providing coverage to more than 200 million Americans, is pleased to submit these comments on behalf of our members.

GENERAL COMMENTS
AHIP and our member plans applaud the efforts of the FDA, and its Center for Devices and Radiological Health's (CDRH's), in performing and publishing these preliminary evaluations to determine the actions necessary to strengthen and improve how it collects and utilizes current scientific evidence and uses that data to revise the 510(k) premarket approval review process. We also support the Institute of Medicine's (IOM's) ongoing review of the 510(k) process, *Public Health Effectiveness of the FDA 510(k) Clearance Process*, which was requested by the FDA, and are confident that it will provide additional insight into areas of high priority for FDA action that will improve the public's access to safe and effective medical devices.

The 510(k) process was created by Congress in 1976, and was intended to more readily make available devices that are safe and effective, and to foster innovation. However lately, due to several recalls of 510(k) devices associated with complications, questions have been raised regarding whether or not consumers are fully protected under the current process. Given the increasing sophistication of medical technology, the current process may no longer strike the most appropriate balance between device innovation and patient safety. Our members have been, and remain, concerned that complex medical devices have been entering the market through the 510(k) process without a comprehensive clinical evaluation of their safety and long term effectiveness, thereby potentially putting patients at greater risk of adverse events.

The preliminary internal evaluations contain recommendations that, if enacted in their entirety, could lead to significant improvement in the safety of medical devices and a reduction in

potential harm for consumers. The FDA acknowledges, and we concur with, the need to continue encouraging innovation and advancements in technology through access to a more transparent evidence base.

We strongly support the preliminary recommendations stated within *Volume II: Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations* as a step to enhance CDRH's knowledge base. This will greatly assist staff in making meaningful changes to the 510(k) premarket clearance processes. In particular, it is important to strengthen the support FDA provides to manufacturers on appropriate and valid clinical trial development, and for the agency to be transparent in its reviews and approval processes. Information collected during the regulatory decision making process should be shared with all stakeholders including consumers, to assist them in making informed health care decisions.

Our members strongly support the preliminary recommendations provided within these two reports, and encourage FDA to act on them in their entirety. In addition, our members have highlighted specific recommendations where we have provided additional comment.

SPECIFIC COMMENTS

510(k) Working Group Preliminary Report and Recommendations

Revise existing guidance to consolidate the concepts of "indication for use" and "intended use" into a single term, "intended use," in order to reduce inconsistencies in their interpretation and application.

We support FDA's effort to clarify the definition and revise existing guidance to decrease discrepancies in the use of the two existing terms during the review process. By clarifying "intended use," along with the recommendation to require a more substantial evidence base with each submission, CDRH will be positioned to make more accurate determinations of "substantial equivalence," in which the device seeking 510(k) clearance has the same intended use as the predicate device.

Consider adopting the use of an "assurance case" framework for 510(k) submissions.

We also support implementing the use of an "assurance case" framework for 510(k) submissions. This framework could help demonstrate validity by providing a convincing statement to show that safety and efficacy claims are met and are supported with relevant evidence.

Develop guidance defining a subset of class II devices, called "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.

We do not support the recommendation to create a new Class II subset, "Class IIb," which would include higher risk 510(k) devices that would need to be supported by additional clinical and manufacturing data, similar to current Class III device review requirements. As we have stated in our prior comments (March 2010) in response to the docket for Strengthening the Center for Devices and Radiological Health's 510(k) Review Process, given the greater potential for catastrophic results in the event of device failure, there should be stricter criteria and processes in place to appropriately classify medical devices as either class II or III.

FDA also should review all class II devices to determine which devices pose potentially significant safety concerns and reclassify them as class III, as appropriate, requiring the manufacturer to submit a higher level of evidence to demonstrate safety and effectiveness (e.g., class II devices, such as drug infusion devices, intraoperative devices, and medical charged-particle radiation therapy systems). In determining which devices pose a greater risk to patients, thereby requiring a more stringent review of the evidence, our members concur with FDA that potential candidates may include some implantable, life-sustaining devices, and/or life-supporting devices, which present greater risks than other class II device types.

Explore greater use of its postmarket authorities, and potentially seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices.

As appropriate, FDA should require more robust levels of post-market surveillance as a condition of clearance for certain devices which have the potential to pose a greater risk to patients. This should also include mandatory adverse event reporting requirements to provide transparent and timely information to physicians, hospitals, consumers and purchasers of health care.

CDRH should continue its ongoing effort to implement a unique device identification (UDI) system.

To assist in the collection of post-market data, our members continue to support FDA in its development and implementation of a unique device identification (UDI) system, as recommended within the evaluation. The creation of a unique device identifier has the potential to reduce medical errors, facilitate recalls, improve reimbursement and inventory control, and reduce product counterfeiting. AHIP strongly supports efforts to more accurately identify and track medical devices and this initiative has the potential to improve the safety and effectiveness of health care for patients, and allow for more accurate post-market surveillance.

Develop guidance on the appropriate use of more than one predicate, explaining when "multiple predicates" may be used. The Center should also explore the possibility of explicitly disallowing the use of "split predicates."

Our members strongly support the CDRH preliminary recommendations to develop separate guidance and regulations to provide greater assurance that any comparison of a new device to a predicate is valid and well-reasoned; when a device should no longer be available for use as a predicate because of safety and/or effectiveness concerns; and clarifying the appropriate use of more than one predicate, explaining when "multiple predicates" may be used. Specifically, we encourage CDRH to no longer allow the use of "split predicates," where manufacturers use one predicate as the basis for a comparison for "intended use" and another predicate as the basis for a comparison for "technological characteristics."

As is the case when using split predicates to prove substantial equivalence, the manufacturer is attempting to prove the safety and effectiveness of its new device using a non-existent "device" whose benefits and harms are unknown. This can lead to unintended, and potentially negative, consequences for patients. We support FDA's efforts to advance the public's health by helping speed innovations to make medicines and devices safer and more effective. However, as currently structured, the 510(k) clearance process relies too heavily on the use of historical predicates to prove safety and effectiveness, instead of current scientific evidence.

Take steps through guidance and regulation to facilitate the efficient submission of high-quality 510(k) device information.

Our members strongly support the recommendation that each manufacturer provide regular, periodic updates to CDRH, listing any modifications made to its device, and providing a clear explanation why each modification did not warrant a new 510(k) submission. Existing guidance also should be used to clarify what types of modifications warrant submission of a new 510(k) application; clarify what situations warrant the submission of manufacturing process information as part of a 510(k), and when it is appropriate to withhold clearance on the basis of a failure to comply with good manufacturing requirements.

Develop guidance and regulations regarding appropriate documentation of transfers of 510(k) ownership

The CDRH should update the 510(k) database to include transfers of 510(k) ownership. Documentation pertaining to transfer of ownership should include any substantial changes in the manufacturing environment and clarify that the transfer does not adversely impact it.

Consider issuing a regulation to define the scope, grounds, and appropriate procedures, including notice and an opportunity for a hearing, for the exercise of its authority to fully or partially rescind a 510(k) clearance.

We fully support FDA issuing a regulation to define when it is appropriate (and the process) to fully or partially rescind a 510(k) clearance. FDA should be allowed to act quickly to protect patients by removing a potentially faulty and dangerous medical device from the market, based on the latest clinical evidence.

Revise existing guidance to streamline the current implementation of the de novo classification process and clarify its evidentiary expectations for de novo requests.

CDRH should look to revise and strengthen the current implementation of the de novo classification process. There remain concerns that some devices cleared through this mechanism are not of low risk to patients and may require more stringent review. While it is understood that very few devices are classified using the de novo process (16 requests received in 2009), allowing any devices into the market that do not have a predicate device for comparison (and without a more stringent premarket approval application) could leave questions of long-term safety and effectiveness unanswered. FDA should develop a more streamlined approach to de novo reviews, outlining strict data and evidence requirements in light of the lack of appropriate predicate comparison.

We applaud FDA's efforts and the multi-stakeholder review activities underway at the IOM to revise and strengthen the 510(k) and other medical device clearance processes. These efforts to improve how current scientific evidence is utilized within the 510(k) clearance process, while increasing the transparency and availability of the data submitted and reviewed by the FDA, will help ensure and maintain the public's trust that the medical devices available in the market place are dependable and safe.

Thank you for the opportunity to provide these comments.

Sincerely,

Carmella Bocchino
Executive Vice President, Clinical Affairs and Strategic Planning

AACC
Improving healthcare through laboratory medicine

2010 SEP 23 A 11:44

September 21, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061,
Rockville, MD 20852.

Docket No. FDA-2010-N-0348

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the Food and Drug Administration's (FDA's) 510(k) Working Groups' Preliminary Report and Recommendations on the Agency's device clearance process. AACC supports the FDA's efforts to clarify and streamline the current 510(k) review mechanism. We believe that clearer, more predictable guidance, in conjunction with needed regulatory reforms, will better serve medical device manufacturers, the health care community, and the public alike.

De Novo Process
The 510(k) Working Group found that "Although there exists an alternative regulatory pathway for devices that lack a clear predicate but whose risks do not warrant class III controls...this pathway, as currently implemented, is inefficient and has not been utilized optimally across the Center." On the basis of this finding, the Group recommends that the FDA "reform its implementation of the de novo classification process to provide a practical, risk-based option that affords an appropriate level of review and regulatory control for eligible devices."

AACC strongly supports the Working Group recommendation. Congress authorized the de novo process to allow the agency to reclassify low risk devices that would automatically be designated as Class III devices, solely because there is no predicate device, as Class I or II. This means that manufacturers, in certain instances, are able to seek clearance through the less burdensome 510(k) process, rather than the more costly and onerous pre-market approval (PMA).

Unfortunately, confusion over evidentiary requirements, along with the length of time associated with Agency review, has discouraged many IVD manufacturers from pursuing this route. In each of the past few years, the Office of Vitro Diagnostic (OIVD) has received only one IVD de novo submission. Since 2005, the length of time for each review has averaged 311 days—50 days longer than the baseline year. We are confident, however, that the number of de novo applications would increase substantially, and the review time decrease, if the process were more clearly defined and predictable.

FDA-2010-N-0348

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The use of the de novo process is particularly important for devices, such as tests for Therapeutic Drug Monitoring (TDM), where consumer demand is often limited, but the potential for improved patient care is significant. Shifting the review of a low volume, low risk test from a PMA to a 510(k) review may make development of a previously unprofitable test, now cost-effective. This change benefits the manufacturer, which now has an incentive to develop and market the test, as well as the patient, who now has access to a valuable test for managing their drug therapy.

Use of Predicate Devices

The Working Group also identified the quality of some predicate devices to be an issue of concern. The panel recommended that "CDRH should explore the development of guidance and regulation to provide greater assurance that any comparison of a new device to a predicate is valid and well-reasoned." AACC agrees with this recommendation. Not all predicate devices are the same. Many are of high quality, but some may be substandard, and possibly not in use anymore. The FDA should ensure that a predicate meets the agency's safety and effectiveness criteria, as well as serves as a valid comparison.

Rescission Authority

The Working Group recommends "that CDRH consider issuing a regulation to define the scope, grounds, and appropriate procedures, including notice and an opportunity for a hearing, for the exercise of its authority to fully or partially rescind a 510(k) clearance. As part of this process, the Center should also consider whether additional authority is needed." AACC supports this approach. The FDA should have clear, established authority to remove a device from the market if it endangers public safety. Additionally, its important for manufacturers to understand what circumstances may trigger an agency action and what options are available for appeal.

By way of background, AACC is the principal association of professional laboratory scientists--including MDs, PhDs and medical technologists. AACC's members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work in hospitals, independent laboratories and the diagnostics industry worldwide. The AACC provides international leadership in advancing the practice and profession of clinical laboratory science and its application to health care. If you have any questions, please call me at (919) 966-3724, or Vince Stine, PhD, Director, Government Affairs, at (202) 835-8721.

Sincerely,

Catherine Hammett-Stabler

Catherine A. Hammett-Stabler, Ph.D., DABCC, FACB
President, AACC

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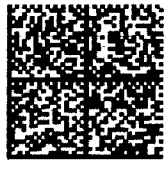

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
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Zimmer, Inc. (Carol Vierling) – Comment (posted 11/02/10)

FDA-2010-N-0348-0066

Zimmer, Inc.

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October 26, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir or Madam,

REF: Docket No. FDA-2010-N-0348

On August 5, 2010, the Food and Drug Administration (FDA) published a request for comments under Docket No. FDA-2010-N-0348. Zimmer attempted to submit comments electronically on October 4 but now realize that our comments were not attached; only the cover email was submitted (tracking number 80b66830).

We regret this mistake and apologize for any inconvenience this has caused. Since we attempted to meet the deadline, we ask that FDA consider our comments (enclosed). Please contact me if further information is needed at 574-372-4964 or at carol.vierling@zimmer.com.

Sincerely,

Carol Vierling
Vice President, Corporate Regulatory Affairs
Zimmer, Inc.

FDA-2010-N-0348

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VOLUME I: 510(k) WORKING GROUP PRELIMINARY REPORT AND RECOMMENDATIONS

1. A Rational, Well-Defined and Consistently Interpreted Review Standard

Recommendation: *CDRH should clarify the meaning of "substantial equivalence" through guidance and training for reviewers, managers and industry.*

Zimmer believes that the 510(k) program can be improved upon with more clarity, consistency and transparency in decision-making. We agree that clarification of some elements of section 513(i) of the Act will benefit stakeholders.

Section 513(i) establishes that a medical device is substantially equivalent to a predicate device if the subject device has *the same intended use* as the predicate device; and (1) it has the same technological characteristics as the predicate device; or (2) it has different technological characteristics which *do not raise new questions of safety and effectiveness* and is shown to be *as safe and effective* as the predicate device. There has been confusion for both reviewers and industry about the meaning of "same intended use" and what questions of safety and effectiveness are considered "new". Zimmer supports clarifying the meaning of these terms through amended regulations and guidance.

Zimmer believes that it is critical that the terms "intended use" and "indications for use" remain separate. Combining the two terms may constrain the meaning of intended use and result in a greater number of Not Substantially Equivalent (NSE) determinations. The Code of Federal Regulations (21 CFR 801.4) provides a definition of intended use in the context of postmarket activities related to the need for adequate directions for use, and indication for use is defined in 21 CFR 814.20. Neither is defined for use in the context of substantial equivalence. Zimmer recommends adding definitions to 21 CFR Part 807 that clarify the use of these terms in the premarket notification context.

Zimmer recommends that 21 CFR Part 807 be amended to include a discussion of

intended use and indications for use. We suggest the following:

New Section 807.80 Meaning of Intended Use and Indications for Use

The words "intended use" in 807.100(b)(1) refer to a regulatory concept that determines the boundaries of use for a generic type of device and is constructed to encompass the appropriate breadth of use for which the regulatory controls for generic device type continue to provide reasonable assurance of safety and effectiveness. The words "intended use" refer to the objective intent for the device function of the persons legally responsible for the proposed labeling of the device that is the subject of the premarket notification submission and describes what the device is intended to provide to the user and patient. For example, the intended use of an intravenous administration set is to deliver fluids to the patient via the circulatory system. Objective intent may be inferred from such persons' written or oral expressions, or the design of the device, however, for the purpose of determining substantial equivalence, the objective intent must be determined from the proposed labeling. The "indications for use" provides a detailed, specific description of the target population(s) for the intended use that is a general description of device function. This includes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate and/or a description of the general or specific patient population(s) for which the device is intended, as appropriate.

For example, the intended use of an electrosurgical cutting and coagulation device is to remove tissue and control bleeding by use of high-frequency electrical current. Electrosurgical cutting and coagulation devices however, may be specifically designed to accommodate different anatomies. They may have indications for use in thoracic, ENT or other procedures.

In regard to indications for use, Zimmer recommends that FDA continue the practice of attaching an "Indications for Use" form to all substantially equivalent (SE) letters. The Indications for Use form provides a transparent means through which all stakeholders are able to clearly identify the indications for use that FDA has cleared. This is important because it provides clarity in limiting promotional activities.

Off-Label Use

Recommendation: *The 510(k) Working Group recommends that CDRH explore the possibility of pursuing a statutory amendment to section 513(i)(1)(E) of the Federal, Food . Drug and Cosmetic Act[21 USC §360c(i)(1)(E)] that would provide the agency with the express authority to consider an off-label use, in certain limited circumstances, when determining the "intended use" of a device under review through the 510(k) process.*

Zimmer agrees that it is important for reviewers and managers to identify when there is a reasonable likelihood that the device will be used for an intended use other than that in the proposed labeling and when that use could cause harm. However, 510(k) review and clearance should not be negatively impacted by potential off-label use. As is common practice, the Agency may require a precaution statement in the labeling that the device has not been studied for a use that is off-label.

Different Questions of Safety and Effectiveness

Recommendation: *The 510(k) Working Group recommends that CDRH reconcile the language in its 510(k) flowchart with the language provided in section 513(i) of the Federal Food, Drug, and Cosmetic Ace [21USC§360c(i]) regarding "different technological characteristics" and "different questions of safety and efficacy".*

Zimmer agrees with the 510(k) Working Group's recommendation that language in the FDA 510(k) flowchart and statutory language in 513(i) of the Act should be reconciled. In accordance with the Act, if a device with the same intended use but different technological characteristics from the predicate, raises "different" questions of safety or

effectiveness compared to the predicate device, the new device cannot be found substantially equivalent. As reflected in Blue Book Memorandum K86-3, the Agency has interpreted the words "different questions" to be "different types of questions". By inserting "types", it is our understanding that the agency was indicating that different questions can be grouped in a manner that provides FDA with appropriate discretion in deciding what scientific questions justify making a new device NSE on this basis.

Zimmer proposes that a question of safety and effectiveness is not "different" if the question can be answered through established, well-recognized test methods. By focusing on what testing is required and pointing to well-established test methods, subjectivity in defining "different" is removed.

Concerns about Predicate Quality

Recommendation: *The 510(k) Working Group recommends that CDRH consider developing guidance on when a device should not longer be available for use as a predicate because of safety and/or effectiveness concerns. It is expected that such a finding would be an uncommon occurrence. Any factors set forth in guidance regarding when a device should no longer be used as a predicate should be well-reasoned, well-supported and established with input from a range of stakeholders, and unintended consequences should be carefully considered.*

Zimmer does not agree with this recommendation, and believes that statutory change is required to disqualify a legally marketed device from being available as a predicate because of safety or effectiveness concerns. New legislation is not necessary since FDA already has authority to remove unsafe or ineffective devices from the market. There are a number of older devices that remain relevant to current standards of care or remain popular because they represent a more affordable option than the latest technology. There also may be attributes of older predicate devices that are relevant to the newer technologies. Finally, Zimmer notes that devices evolve as new technological advances are made, and are not expected to be identical to the older predicate devices.

Rescission Authority

Recommendation: *The 510(k) Working Group recommends that CDRH consider using a regulation to define the scope, grounds and appropriate procedures, including notice and an opportunity for a hearing, for the exercise of its authority to fully or partially rescind a 510(k) clearance. As part of this process, the Center should also consider whether additional authority is needed.*

Zimmer does not believe that a regulation defining CDRH's authority to rescind a 510(k) is needed nor do we believe that the Center needs this additional authority. FDA has numerous tools to remove violative products from the market, including banning the device in situations of substantial deception or unreasonable risk of illness or injury, per Section 516 of the Act. FDA may also issue an order for mandatory device recall pursuant to Section 518 of the Act and may, when necessary, obtain court orders for product seizure.

If a predicate device is rescinded for reasons unrelated to safety and efficacy, it could result in each subsequent device that cited the rescinded device as a predicate being removed from the market. This would cause a potentially significant impact to public health. FDA should use the tools currently under its authority to remove an unsafe or ineffective device from the market.

Use of "Split Predicates" and "Multiple Predicates"

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance on the appropriate use of more than one predicate, explaining when "multiple predicates" may be used. The Center should explore the possibility of disallowing the use of "split predicates". In addition, the Center should update its existing bundling guidance to clarify the distinction between multi-parameter or multiplex devices and bundled submissions.*

Recommendation: *The 510(k) Working Group recommends that CDRH provide training for reviewers and managers on reviewing 510(k)s that use "multiple predicates", to better assure high-quality review of these often complex devices. The training should clarify the distinction between multi-parameter or multiplex devices and bundled submissions. In addition, CDRH should more carefully assess the impact of submissions for multi-parameter or multiplex devices and bundled submission on review times, and should consider taking steps to account for the additional complexity of these submissions as it establishes future premarket performance goals.*

Zimmer believes that the use of multiple predicates, i.e., using more than one predicate where each predicate individually supports substantial equivalence and both predicates fall with the same type of device, is and should continue to be permissible under the 510(k) process. A 510(k) submission utilizing multiple predicates must still provide a clear demonstration of safety and effectiveness. We disagree with the 510(k) Working Group proposal.

Zimmer supports training for reviewers and managers on reviewing 510(k)s that use multiple predicates to address the apparent confusion within the Agency. We also support development of additional guidance on bundling to provide more clarity on multi-parameter or multiplex devices and bundled submissions.

The 510(k) Report notes that bundled submissions are often more complex than non-bundled submissions or require additional resources within or outside of CDRH and therefore, require more review time than non-bundled submissions. CDRH should evaluate the additional resources it requires to review bundled submissions within the currently agreed upon performance goal and then propose a commensurate increase in user fees to provide the needed resources for this type of submission.

Evaluation of Automatic Class III Designation (*De novo*)

Recommendation: *The 510(k) Working Group recommends that CDRH should reform its implementation of the de novo classification process to provide a practical, risk-based*

option that affords an appropriate level of review and regulatory control for eligible devices.

Strengthening and optimizing the *de novo* process through a well-defined regulatory pathway will benefit the agency, industry and patients. This underutilized process has the potential to play a key role in the regulation of medical devices lacking a predicate, for which general or special controls provide a reasonable assurance of safety and effectiveness.

Zimmer recommends that FDA eliminate the need to submit a 510(k) and receive an NSE determination before requesting *de novo* classification so that it becomes a "one-step" process rather than a two-step process. As part of the one-step process, FDA should implement use of a pre-review process for a *de novo* submission where FDA and the manufacturer agree to use the *de novo* process and to the content requirements of the *de novo* submission.

2. **Well-informed Decision Making**

Recommendation: *The 510(k) Working Group recommends that CDRH should take steps through guidance and regulation to facilitate the efficient submissions of high-quality 510(k) device information, in part by better clarifying and more effectively communicating its evidentiary expectations through the creation, via guidance, of a new "class IIb" device subset.*

Zimmer does not support a formal Class IIb. However we do agree with the concept of identifying a small subset of Class II devices, as was laid out by AdvaMed, for strengthening the 510(k) process by providing enhanced transparency and predictability to the CDRH reviewer expectations for a small, focused subset of higher risk Class II devices. However, we are concerned that the scope of the products proposed by FDA is too broad and the proposed requirements, when considered in their totality, are overly

and unduly burdensome for Class II devices.[1]

The term "IIb" has no legal definition and implies a distinction that does not exist. Therefore, as this proposal is further developed, we urge CDRH to change its terminology and its focus from "Class IIb" to "a subset of Class II" and a consideration of a risk-based guidance for evidentiary standards for specific device types. This shift would make clear that this is not a new classification scheme, but simply a risk-based guidance that provides clearer direction for submissions for certain life saving and life sustaining device types within the current Class II program. Because these appropriately identified devices will require additional resources by both industry and FDA, it is important that they are limited to a small number of higher risk devices where public safety will benefit from the extra expenditure of resources, otherwise the extra requirements will not be practically implementable and will detract from the focus on the truly higher risk devices.

Defining clear criteria and standards that should apply, through a public notice and comment period, for determining which devices types fall within this higher risk subset is a necessary step. The types of devices that would fall into this subset would be determined based on risk management processes, and could include life-sustaining devices and life-supporting devices where the potential for increased concern exists such that special requirements are appropriate to assure the safety and effectiveness of these devices and to clarify data expectations for manufacturers seeking clearance for devices in these classes. As more experience is gained and the use of each device becomes well-established with a historical track record of safe and effective use, the device would be removed from the subset. Thus, effectively establishes a sub-tier of regulation for a limited and dynamic subset of devices subject to 510(k) clearance. **However, devices with a record of safety in clinical use or with up-to-date standards, guidance and/or**

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[1] In its August 31, 2010 webinar the Agency conveyed that all devices for which FDA requests clinical data would be included in Class IIb.

special controls that have proven effective would not warrant placement in the higher risk subset.

Unreported Device Modifications

Recommendation: *The 510(k) Working Group recommends that CDRH revise existing guidance to clarify what types of modifications do or do not warrant submission of a new 510(k), and for those modifications that do warrant a new 510(k), which modifications are eligible for a Special 510(k).*

Zimmer believes that the Special 510(k) process is an efficient and effective mechanism to gain clearance for minor modifications to the manufacturer's own legally marketed device. The manufacturer's certification to design controls assures that appropriate processes have been followed for assessing the significance of changes to the device. Revision of the existing guidance document to clarify the types of device modifications that warrant submission of a new 510(k) would be helpful.

Recommendation: *The 510(k) Working Group recommends that CDRH explore the feasibility of requiring each manufacturer to provide regular, periodic updates to the Center, listing any modifications made to the device without the submission of a new 510(k), and clearly explaining why each modification noted did not warrant a new 510(k). The Center could consider phasing this requirement, applying it initially to the "class IIb" device subset described in Section 5.2.1.3 of the Report, for example, and expanding it to a larger set of devices over time.*

The examples stated in the Report refer to misuse of the Special 510(k) program. If the Special 510(k) program is being misused and additional information is necessary to determine SE, CDRH converts the submission to a Traditional 510(k). Zimmer believes that the recommendation for periodic reports will be overly burdensome for both CDRH and industry if implemented for all Class II devices.

Quality of Submissions

Lack of Clarity

Recommendation: *The 510(k) Working Group recommends that CDRH consider adopting the use of an "assurance case" framework for 510(k) submissions.*

As FDA points out in its recommendations, the "assurance case" framework is not one that is currently in use in the medical device industry, either by companies or by FDA. This raises two immediate concerns to the industry. First, given that CDRH clearly indicates that lack of adequate reviewer and industry training is a general concern relevant to the current perceived inconsistency of 510(k) reviews, this would impose yet another new training requirement on a Center that is already struggling with turnover of personnel. The second concern is the lack of clarity about the problem that is leading FDA to make this recommendation and whether the "assurance case" is the only or best means of addressing the problem.

The example cited by FDA in support of the use of the "assurance case" is one where a labeling change in an earlier generation of device was not sufficiently highlighted by the submitter and the reviewer overlooked the change in making a substantial equivalence determination. The FDA Working Group states that all intended use information should be submitted and described in detail in a single section of the 510(k). That simple recommendation would be easy to implement and would require very little in the way of additional training for reviewers or industry. The FDA working group also repeats the long-standing expectation that 510(k)s should describe any modifications made to a device since its previous clearance. Even without the use of an "assurance case," these two simple changes would provide that any modifications to a device would appear in two sections of any future 510(k), thus limiting the likelihood that they would be overlooked by FDA reviewers. Accordingly, Zimmer does not support this recommendation.

Recommendation: *The 510(k) Working Group recommends that CDRH explore the possibility of requiring each 510(k) submitter to provide as part of its 510(k) detailed photographs and schematics of the device under review in order to allow review staff to develop a better understanding of the device's key features.*

Zimmer agrees that photographs and schematics would allow review staff to develop a better understanding of the device under review. We often include detailed diagrams in the body of the submission just for this purpose. We are concerned about releasing confidential or proprietary information, however. Any photographs or graphic depictions of a device that would provide proprietary information to competitors, both domestic and outside the United States, therefore, should not be released to a public website or otherwise be made publically available.

Recommendation: *The 510(k) Working Group recommends that CDRH should explore 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 so the reviewer could, as needed, examine the device hands-on as part of the review of the device itself or during future reviews in which the device in question is cited as a predicate.*

Zimmer understands the benefits of requesting submitters to keep one unit of the device available for CDRH examination during the 510(k) review process. However, CDRH must consider the logistics related to such a request if the device is sent to FDA. Large pieces of equipment will require loading dock/receiving areas as well as secure storage with an appropriate storage environment. If CDRH expects equipment to be operational, it may require special installation and calibration activities. Devices such as x-ray equipment, robotic surgical equipment, and sterilization equipment would be expensive to ship; require installation by specialized technicians; and would occupy a large amount of space at CDRH.

CDRH must recognize that the sample would not be a product of the standard manufacturing process, but may be a prototype or functional model built for the review process or other demonstration purposes. In some cases, the device in its final form may not exist at the time of 510(k) submission. In general, manufacturers are not "in production" of a device that is not cleared by CDRH. Due to the many logistical issues as well as the possibility that a device may not be in its final configuration or not available at all, Zimmer suggests that the availability of a sample device during the review is a CDRH *request* and not a requirement.

Keeping a device available indefinitely so it can be examined when it is cited as a predicate is impractical and would provide limited benefit. Providing the space necessary to ensure secure storage with appropriate environmental conditions would present a financial and logistical burden on industry, especially on small companies with limited facilities. Indefinite retention of devices, especially IVD products, with limited shelf-lives would not provide an accurate representation of the device after the use-before date has passed. In some cases, minor changes are made to devices during their marketed life. Retaining a sample of each version of the device would add to the storage burden.

Improper Recognition of Standards [Abbreviated 510(k)s]

Recommendation: *The 510(k) Working Group recommends that CDRH provide additional guidance and training for submitters and review staff regarding the appropriate use of consensus standards, including proper documentation with a 510(k). CDRH should also consider revising the requirements for "declaration of conformity" with a standard, for example by requiring submitters to provide a summary of testing to demonstrate conformity, if they choose to make use of a "declaration of conformity."*

Zimmer strongly supports the recommendation that CDRH provide additional guidance and training for industry and review staff regarding the appropriate use of consensus standards, including proper documentation within the 510(k).

Existing FDA guidance on "Recognition and Use of Consensus Standards" addresses many of the issues noted in the 510(k) Report, and additional education on these topics would be particularly helpful to industry and FDA review staff.

Additionally, the guidance clearly notes that falsifying a declaration of conformity is a prohibited act under 21 U.S.C. 331(x). Therefore, requiring all submitters to provide a summary of testing to demonstrate conformity, even when the standard contains pass/fail criteria, if they choose to make use of a "declaration of conformity", is unnecessary. This would undermine the basic tenet of the Abbreviated 510(k) process, which is another important and valuable part of the 510(k) Program.

Incomplete Information

Recommendation: *The 510(k) Working Group recommends that CDRH should consider revising 21 CFR 807.87 to explicitly require 510(k) submitters to provide a list and brief description of all scientific information regarding the safety and/or effectiveness of a new device known to or that should be reasonably known to the submitter. The Center could then focus on the listed scientific information that would assist it in resolving particular issues relevant to the 510(k) review.*

As CDRH is aware, AdvaMed's proposal for a subset of class II devices, which included enhanced submission requirements, called for a summary of technical and clinical information. AdvaMed felt this would be appropriate for those devices that are higher risk and whose uses and technologies are not well-characterized, that lack a record of safety in use, or that do not have effective and up-to-date standards, guidance, and/or special controls. In its preliminary internal evaluation report, the FDA Working Group did, in fact, recognize that "it *may* be necessary for a submitter to include clinical or other scientific information..." (emphasis added). This statement suggests that it will not always be necessary for this information to be provided. Zimmer agrees that the

expansion of this requirement to all class II, and those class I devices on the reserve list, is excessive, as well as suggestive of current PMA requirements.

Routine submission of both a listing and a description of all scientific information for all 510(k)s would be burdensome on both industry and CDRH, with unclear benefit. Least burdensome requirements do apply to 510(k) submissions and should be applied to this specific recommendation. The scope of this recommendation, as noted above, should be limited to a specified high-risk subset of class II devices, where the information may be relevant to a determination of substantial equivalence.

The example CDRH provides in its report of the need for all scientific information indicates a situation where a submitter omitted data from three clinical studies that contradicted the studies submitted in support of the 510(k). We feel that it is unlikely that requiring submission of all scientific information for all 510(k)s would address this type of situation. In fact, this example is adequately covered by the Truthful and Accurate Statement that companies are required to sign with each 510(k) submission. Manufacturers understand the implications of submitting a false statement of truthfulness and accuracy and are quite diligent at assuring that the totality of information submitted in a 510(k) fairly represents the safety and effectiveness of the new device. One must assume that, in a situation like the one depicted by FDA, where a company knowingly excludes information that is relevant to substantial equivalence and directly contradictory to the data submitted in the 510(k), FDA will take action against the company based on its failure to meet the requirements of the Truthful and Accurate Statement.

Prior to CDRH revising 807.87, hopefully to address a subset of Class II devices, it would be helpful to consider the types of information that would be most useful to reviewers in making a substantial equivalence determination. It seems clear from the example provided that CDRH is seeking information not publicly available and found within the submitter's internal documents, such as additional clinical studies and information from the Design History File directly relevant to the device being reviewed.

It also would be reasonable to ask a submitter to include a brief summary of information from market experience with the same device in markets outside the US, if any. CDRH itself has access to information in published, peer reviewed literature, as well as information on MDRs and recalls which, in the case of a new device not yet on the market in the US, would not be relevant. It is not clear from the recommendation whether a summary of this type of publicly available information would be expected as part of a listing and brief description of all scientific information.

A final consideration for CDRH is whether a requirement for all scientific information could be implemented without statutory change. FDA may request scientific information regarding safety and effectiveness about a device when that information can be shown to be germane to the substantial equivalence determination. If the information is not necessary to make a substantial equivalence determination, FDA may not request it without a statutory change.

In conclusion, Zimmer supports the requirement, for a subset of Class II devices, to include a summary of technical and clinical information in a 510(k) for a new device. We believe it would be appropriate for the Agency to provide clarity regarding its expectations, so that companies could provide the complete information needed in a timely fashion. We also strongly recommend that the requirement for scientific information not be overly broad and address only information directly relevant to the safety and effectiveness of the new device.

Type and Level of Evidence Needed

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance defining a subset of class II devices, called "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.*

Zimmer does not support a formal Class IIb. However we do agree with the concept of identifying a small subset of Class II devices, as was laid out by AdvaMed, for strengthening the 510(k) process by providing enhanced transparency and predictability to the CDRH reviewer expectations for a small, focused subset of higher risk Class II devices. This proposal is, in fact, complementary to device-specific guidance documents CDRH has issued in the past for Class II device 510(k) submissions, examples which include surgical sutures, total joint implants and intravascular administration sets.

Defining clear criteria and standards that should apply, through a public notice and comment period, for determining which devices types fall within this higher risk subset is a necessary step. The types of devices that would fall into this subset would be determined based on risk management processes, and should generally be limited to life-sustaining devices and life-supporting devices where the potential for increased concern exists such that special requirements are appropriate to assure the safety and effectiveness of these devices and to clarify data expectations for manufacturers seeking clearance for devices in these classes.

Recommendation: *The 510(k) Working Group further recommends that CDRH develop and implement training for review staff and industry regarding the delineation between "class IIa" and "class IIb."*

Delineation between class IIa and class IIb implies a new classification structure which is beyond the current statutory authority of the Agency. As the guidance under the "class IIb scheme" is developed, it must be made clear to both the review staff and industry that this is not considered device reclassification. The term "subset of Class II" would be preferred to the "Class IIb" terminology proposed. Once the criteria and process for a "subset of Class II" is developed, Zimmer would encourage training of review staff and industry on the application and implementation.

Clinical Information

Recommendation: *The 510(k) Working Group recommends that CDRH, as part of the "class IIb" guidance described above, provide greater clarity regarding the circumstances in which it will request clinical data in support of a 510(k), and what type and level of clinical data are adequate to support clearance. CDRH should, within this guidance or through regulation, define the term "clinical data" to foster a common understanding among review staff and submitters about types of information that may constitute "clinical data." General recommendations related to the least burdensome provisions, premarket data quality, clinical study design, and CDRH's mechanisms for pre-submission interactions, including the pre-IDE and IDE processes, are discussed further in the preliminary report of the Center's Task Force on the Utilization of Science in Regulatory Decision Making (described further in Section 2, below). That report also recommends steps CDRH should take to make well-informed, consistent decisions, including steps to make better use of external experts.*

In the context of a "subset of Class II" submission, Zimmer supports this recommendation. This recommendation should only apply to those devices that require clinical data to establish substantial equivalence. Additional clarity on CDRH definition and expectations of clinical data (clinical literature vs. clinical study) in this guidance would be welcome.

Postmarket Information

Recommendation: *The 510(k) Working Group recommends that CDRH explore greater use of its postmarket authorities, and potentially seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices. If CDRH were to obtain broader authority to require condition-of-clearance studies, the Center should develop guidance identifying the circumstances under which such studies might be appropriate, and should include a discussion of such studies as part of its "class IIb" guidance.*

In the context of a "subset of Class II" submission, Zimmer supports the recommendation to explore greater use of its postmarket authorities. The FDA currently can request post-market data through FD&C section 522, or in the case of special controls through performance standards, postmarket surveillance, and patient registries. Periodic review of new safety data should be performed to reduce reporting requirements of "subset of Class II" devices when sufficient post-market data are available.

Zimmer does not support the recommendation to "potentially seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices." In light of the existing authority to include postmarket studies in premarket special controls and through section 522, further authority is unnecessary.

Manufacturing Process Information

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance to provide greater clarity regarding what situations may warrant the submission of manufacturing process information as part of a 510(k), and include a discussion of such information as part of its "class IIb" guidance.*

Zimmer supports this recommendation only for specific device types within the subset for which specific circumstances or conditions would require the submission of manufacturing information. Zimmer does not support requiring the submission of this information for all device types in the subset of Class II.

Recommendation: *The 510(k) Working Group further recommends that CDRH clarify when it is appropriate to use its authority to withhold clearance on the basis of a failure to comply with good manufacturing requirements in situations where there is a substantial likelihood that such failure will potentially present a serious risk to human health, and include a discussion of pre-clearance inspections as part of its "class IIb" guidance.*

Zimmer supports the recommendation regarding the Agency's authority to withhold clearance as long as that authority is dependent upon a "finding" of Good Manufacturing Practices (GMP) violations that are (i) related to the submitted device; (ii) substantially likely to potentially present a serious risk to human health and (iii) discovered during a routine or "for cause" inspection (not a pre-clearance inspection) resulting in "Official Action Indicated". Given the significance of the consequences of that finding, we believe the Agency should provide a process to notify the sponsor and allow a response prior to the Agency taking action on the finding. We recommend that the Agency define this process and clarify when a clearance should be withheld based upon determinations of GMP violations.

Zimmer does not support including requirements for routine pre-approval inspections for the subset of Class II devices. Section 510(k) is a classification provision and not an approval authority. As such, and unlike PMA safety and effectiveness determinations, pre-clearance inspections have no relevance to the substantial equivalence question.

Lack of Ready Access to Final Device Labeling

Recommendation: *The 510(k) Working Group recommends that CDRH revise existing regulations to clarify the statutory listing requirements for submission of labeling. CDRH should also explore the feasibility of requiring manufacturers to electronically submit final device labeling to FDA by the time of clearance or within a reasonable period of time after clearance, and also to provide regular, periodic updates to device labeling, potentially as part of annual registration and listing or through another structured electronic collection mechanism. If CDRH adopts this approach, updated labeling should be posted as promptly as feasible on the Center's public 510(k) database after such labeling has been screened by Center staff to check for consistency with the device clearance. The Center should consider phasing in this requirement, potentially starting with only a subset of devices, such as the "class IIb" device subset described above, or with a particular section of labeling. CDRH should also consider posting on its public*

510(k) database the version of the labeling cleared with each submission as "preliminary labeling," in order to provide this information even before the Center has received and screened final labeling.

Zimmer does not support this recommendation as stated. The creation of a 510(k) labeling database is duplicative of efforts already underway within the Unique Device Identifier (UDI) System. The Working Group's assumption of benefits to medical professionals and device users are overstated. Creation of a 510(k) labeling database in isolation ignores existing Class III PMA device labeling requirements. Editorial checks of redlined copy by CDRH review staff will require a significant investment of resources (both human and technological) without benefit to the public health. Labeling of some devices contains information that should not be available to the public (such as how to program some electrical devices), and public posting of labeling or preliminary labeling would provide undue benefit to competitors and would inhibit US innovation. Zimmer strongly feels that dissemination of labeling to patients or clinicians should be the responsibility of the manufacturer. General public access to that labeling would lead to further public confusion if the labeling dissemination is not controlled by the manufacturer.

510(k) Summaries

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance and SOPs for the development of 510(k) summaries to assure they are accurate and include all required information identified in 21 CFR 807.92. The Center should consider developing a standardized electronic template for 510(k) summaries.*

Zimmer strongly supports CDRH's development of a guidance and SOPs for 510(k) summaries. In fact, in its March 19, 2010 comments to Docket No. FDA-2010-N-0054, AdvaMed recommended that FDA establish guidance to augment its regulations regarding 510(k) Summary content and ensure compliance to the requirements. It was

suggested that FDA consider providing a template, to assure that the quality of information in 510(k) Summaries is consistent and complete. This will help companies to determine whether a particular device can be used as a predicate, as well as assisting companies in determining the data and other information they will need to include in their own 510(k)s.

In order to avoid redundant work, Zimmer recommends that the summary provided by the manufacturer be used as the basis for the reviewer summaries for 510(k)s and that the requirements for 510(k) Summaries and Reviewer Summaries be made as consistent as possible. This also will help to eliminate discrepancies between the two summaries. CDRH would, of course, have the option of revising, or asking the submitter to revise information as appropriate. In addition, the decision summary would contain additional information related to how the reviewer determined the substantial equivalence of the device that is the subject of the 510(k) submission. The summary also would reflect additional information provided during the review process.

Finally, Zimmer supports eliminating the option for submitters to provide a 510(k) Statement in lieu of a 510(k) Summary. This will assure that consistent and high quality information about a new or modified device will be readily available to the public.

Product Codes

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance and SOPs for the development and assignment of product codes, in order to standardize these processes and to better address the information management needs of the Center's staff and external constituencies. The Working Group also recommended that CDRH enhance existing staff training on the development and assignment of product codes.*

Zimmer agrees with this recommendation. Currently, there is no mechanism to notify industry when a new product code has been established. Standardizing the process of

development and assignment of product codes along with communication about the availability of new product codes will provide transparency of the process and inform industry when there is an addition.

510(k) Databases

Limited Tools for Review Staff and Outside Parties

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance and SOPs for the development of 510(k) summaries to assure they are accurate and include all required information identified in 21CFR 807.92.*

Although it was not specifically stated in the 510(k) Working Group Recommendations, the value of a reviewer "decision summary" was discussed in the text of the report. Zimmer agrees with CDRH comments that "publically providing accurate and meaningful information about previous 510(k) decisions and predicate devices is essential to increasing the transparency and predictability of CDRH's 510(k) decision making." We also agree with CDRH's position that providing information about the basis for previous decisions can provide much-needed clarity about CDRH's evidentiary expectations and decision-making rationale.

Zimmer believes FDA should prepare and post an Office of Device Evaluation (ODE) 510(k) decision summary as Office of *In Vitro* Diagnostics (OIVD) does currently. The decision summary, in combination with complete 510(k) submission summaries, would provide interested parties, including FDA reviewers, third party reviewers, clinicians and industry with meaningful information about the subject of the submission and the predicate device(s). A decision summary would improve consistency in 510(k) decision-making among reviewers, and when updated guidance is lacking, enable manufacturers to understand current clearance requirements for their device.

Although it was not specifically stated in the 510(k) Working Group Recommendations, the value of a reviewer "decision summary" was discussed in the text of the report. Zimmer agrees with CDRH comments that "publically providing accurate and meaningful information about previous 510(k) decisions and predicate devices is essential to increasing the transparency and predictability of CDRH's 510(k) decision making." We also agree with CDRH's position that providing information about the basis for previous decisions can provide much-needed clarity about CDRH's evidentiary expectations and decision-making rationale.

To minimize redundancy and maximize efficiency, the content and format of the decision summary should complement, not repeat, information contained in the 510(k) Summary. If standard content and format for 510(k) Summaries are established, a complementary content and format can be established for reviewer decision summaries.

Limited Information on Current 510(k) Ownership

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance and regulations regarding appropriate documentation of transfers of 510(k) ownership. The Center should update its 510(k) database in a timely manner when a transfer of ownership occurs.*

Zimmer supports this proposal and believes that the complete history of 510(k) ownership should be maintained. We believe that it will be helpful not only for the U.S., but also for foreign registration of devices. It also would be valuable for CDRH to show the full chain of 510(k) ownership and to re-issue 510(k) clearance letters when ownership changes.

We urge FDA to follow through on this recommendation. We also suggest that, if possible, implementation should be handled through an existing and familiar process such

as registration and listing. Implementing the recommendation in this manner would place the information in an existing database, and would simplify both FDA's entry of the information and the public's access to the information.

3. Continuous Quality Assurance

Recommendation: *CDRH should enhance training, professional development, and knowledge-sharing among reviewers and managers, in order to support consistent, high quality 510(k) reviews.*

Zimmer agrees with the approach noted multiple times in the proposals that a key to successful implementation of any change is the proper development and delivery of appropriate training. We also agree that well-designed and delivered training will lead to the greatest likelihood of program success and should be directed at both the CDRH staff and the industry.

In addition, Zimmer has several suggestions for the best way to implement the training. First, we believe that "train the trainer" approaches work well for adult education and that there are several groups that FDA should consider utilizing in this way. External experts from academia and FDA alumni should be considered as potential partners to fill the training needs that will result from the changes being proposed to the 510(k) program. We believe that having training come from outside the program will ensure that it is delivered in a balanced and dispassionate way as well as not take excessive staff time to perform the number of training sessions that will be required to accomplish these changes.

Zimmer recommends that staff training require testing or proof of proficiency, similar to the requirements for training industry staff on QSR procedures. We also believe that this training should be required before staff is empowered to perform reviews or assessments under any new procedures. Again, this also parallels industry training requirements.

Lastly, we are in complete agreement that FDA Vendor Days and other ways to familiarize the staff with various technologies are an important addition to the program. Site visits to industry should be expanded and site visits to academia should be added to the current programs. We support fully the idea that more engagement with scientific experts from all over the world would be a benefit to FDA as well as to industry.

Recommendation: *CDRH should enhance its systems and program metrics to support continuous quality assurance.*

Zimmer strongly endorses the idea of developing a set of metrics to assure continuous quality assurance of the 510(k) review program. We believe that metrics carefully designed to evaluate specific aspects of the program will provide clear guidance to the agency for maintaining and improving the effectiveness of the program.

It is important to note, though, that construction of these metrics will not be easy. Each metric should be focused on a specific question or aspect of the program. Collectively and individually, they need to be simple and unambiguous both to FDA staff and to other stakeholders. Finally, they must be pursued diligently, and the results should be made public in a timely manner.

Finally, should FDA develop a recommendation or proposal to modify the system based on the results shown by one of the metrics, FDA will need to demonstrate clearly the causal relationship between the recommendation and the metric. In other words, changes that FDA proposes should be traceable to results of the metrics that they establish.

VOLUME II: UTILIZATION OF SCIENCE IN REGULATORY DECISION MAKING

Zimmer has chosen to comment on those recommendations from the Task Force on the Utilization of Science in Regulatory Decision Making Report that, in our view, are most important. Our comments are noted below, beginning with point 3 of the Report.

3. Promptly Communicating Current or Evolving Thinking to All Effected Parties

Recommendation: *CDRH should make use of more rapid communication tools to convey its current thinking and expectations.*

Recommendation: *The Task Force recommends that CDRH continue its ongoing efforts to streamline its processes for developing guidance documents and regulation, consistent with the Center's FY 2010 Strategic Priorities.*

We support the development of additional product specific guidance and training for FDA staff and industry. However, increased issuance of Level 1 guidance raises concerns about implementation of new expectations without adequate notice to affected stakeholders is a problem in the real world of product and submission development. At any one time, there will be products in various stages of development, including submissions pending at the Agency, applications ready for submission to the Agency, and existing device trials near completion. There is a real need for notice and comment on guidance documents, and therefore the use Level 1 guidance is best reserved for only those matters where there is an urgent and documented public health issue that must be immediately addressed. The gains in streamlining the Agency's guidance implementation process through increased issuance of Level 1 guidance seem to be modest and deprive due process of stakeholder involvement.

Additionally, there should be more extensive engagement in the development of guidance, such as placing FDA staff on joint teams with stakeholders, including industry.

health care providers with product knowledge, and academic experts to develop first drafts of needed guidance. Although guidance documents are not legally binding on the Agency, they do "represent the Agency's current thinking", and are relied upon by FDA review staff, device companies and other public entities. Because of the importance of these documents, the Agency would be better served if it were fully informed on the issues at hand, by receiving stakeholder and individual expert feedback, prior to publishing a draft guidance document. Obtaining this type of feedback should not be limited to public meetings or workshops; the Agency could meet with selected stakeholders and experts individually, and should do so when such meetings will advance the guidance development process. *See* 21 C.F.R. § 10.115(g)(1)(i) ("FDA can seek or accept early input from individuals or groups outside the Agency.").

Further, to maximize the value and efficiency of the acceptance of stakeholder guidance, we recommend the Agency more clearly indicate those guidance document topics in which receipt of early draft versions will expedite the development process versus those areas in which the Agency is well down the path in developing a draft guidance document. To increase transparency, the Agency should provide feedback on information and drafts it receives from outside sources.

Recommendation: *The Task Force recommends that CDRH establish as a standard practice sending open "Notice to Industry" letters to all manufacturers of a particular group of devices for which the Center has changed its regulatory expectations on the basis of new scientific information. CDRH should adopt a uniform template and terminology for such letters, including clear and consistent language to indicate that the Center has changed its regulatory expectations, the general nature of the change, and the rationale for the change.*

Zimmer supports the Agency's recommendation to establish a standard practice for Notice to Industry letters (NTI) for use in conveying information for which the Center has changed its regulatory expectations on the basis of new science.

As part of the standard practice, we recommend the Agency clearly define the types of information and circumstances in which it would be appropriate to issue a NTI. Use of NTIs to communicate changes in thinking related to product specific issues impacting safety or effectiveness has the potential to improve the current process, where currently such issues may be communicated only to individual companies already under review. Overuse of NTIs to communicate procedural topics, such as application format, or other topics which can be addressed via Level 2 guidance will minimize the effectiveness of the NTIs and cause unnecessary complexity to the process. Clearly defining the types of content to communicate via NTIs will maximize the utility and effectiveness of NTIs.

A critical aspect of the NTI standard practice should be a recognition that at any one time when the Agency issues a NTI, there will be products in various stages of development, including submissions pending before the Agency, applications ready for submission to the Agency, or existing device clinical trials near completion. Because of these real-world situations, it is important that the NTI standard practice include a mechanism for phasing in the new requirements or accepting alternate but equivalent measures. Under current practice, issuance of a final guidance sets forth the Agency's current thinking, but recognizes that other mechanisms may exist for addressing the particular concern. This approach should continue to apply to NTIs, thus allowing a company to address the concern in another manner.

In addition to opening a docket along with the issuance of an NTI, we recommend the Agency consider establishing a timeframe for reviewing comments submitted to the docket. Following issuance of the NTI, the Agency should work to incorporate the new information into draft guidance for review and comment.

We agree with the recommendation of providing the letters to all manufacturers of a particular group of devices for which the Center has changed its regulatory expectations. Importantly, the Agency should use additional communication tools to the industry in general, so that companies contemplating moving into the particular device space have

visibility to the change in Agency thinking. Specifically, we recommend posting on the CDRH website NTIs in a readily accessible manner and tagging NTIs for inclusion in the CDRH email, "What's New at CDRH Update."

Further, a webpage dedicated to topics related to new science is certainly an important step to increasing transparency and understanding. Inclusion and consolidation of the NTIs on this page along with the standard operating procedure that governs NTI development is recommended. We do recommend that the web page be created so that it is readily accessible, consolidates all new science information in one location and minimizes the use of multiple links to obtain the information, which decreases the ability to locate information.

Lastly, we believe adoption of a standard process for creating and issuing NTIs should not preclude the Agency from communicating anticipated changes in thinking at a pre-IDE meeting or other pre-submission meetings if the NTI is still under review within the Agency. One can envision a situation where a company leaves a pre-IDE meeting with an understanding of a path forward, only to receive a NTI shortly after the meeting. Steps to avoid such situations benefit the Agency and its stakeholders.

Recommendation: *The Task Force recommends that CDRH take steps to improve medical device labeling, and to develop an online labeling repository to allow the public to easily access this information. The possibility of posting up-to-date labeling for 510(k) devices online is described in greater detail in the preliminary report of the 510(k) Working Group.*

Zimmer does not agree with the recommendation to develop an online labeling repository if the repository is for prescription medical devices. Labeling supplied with prescription medical devices is intended for the physician or other healthcare provider and not the general public. In the case of total joint arthroplasty devices, instructions on implantation would have no meaning to the lay person and may create public confusion.

As noted previously, the creation of a 510(k) labeling database is duplicative of efforts already underway within the Unique Device Identifier (UDI) System. Zimmer strongly feels that dissemination of labeling to patients (direct when appropriate or through the attending clinician) and to clinicians should remain the responsibility of the manufacturer thereby ensuring the information reaches the appropriate audience and does not cause confusion.

Postmarket Oversight

Recommendation: *The Task Force recommends that CDRH continue ongoing efforts to develop better data sources, methods, and tools for collecting and analyzing meaningful postmarket information, consistent with the Center's FY 2010 Strategic Priorities. In addition, the Center should conduct a data gap analysis and a survey of existing U.S. and international data sources that may address these gaps. These efforts should be in sync with and leverage larger national efforts. As CDRH continues its efforts to develop better data sources, methods, and tools, it should invite industry and other external constituencies to collaborate in their development and to voluntarily provide data about marketed devices that would supplement the Center's current knowledge.*

Zimmer supports this recommendation. To achieve this goal, however, the UDI system must be established and implemented, data management systems must be compatible and up to date and duplicative efforts must be avoided.

Recommendation: *The Task Force recommends that CDRH conduct an assessment of its staffing needs to accomplish its mission-critical functions. The Center should also work to determine what staff it will need to accommodate the anticipated scientific challenges of the future. CDRH should also take steps to enhance employee training and professional development to assure that current staff can perform their work at an optimal level. As part of this process, the Center should consider making greater use of professional development opportunities such as site visits or other means of engagement*

with outside experts in a variety of areas, including clinical care, as described below. This recommendation complements the Center's ongoing efforts under its FY 2010 Strategic Priorities to enhance the recruitment, retention, and development of high-quality employees.

Zimmer supports this recommendation. We encourage CDRH to determine essential functions that support the FDA priorities of supporting public health and access to improved medical treatment and focus resources on these functions. Recruitment and development of highly qualified, well-trained and motivated employees are essential in achieving CDRH goals.

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MedTech (Heather Erickson) – Comment (posted 11/02/10)

FDA-2010-N-0348-0067

MedTech

September 29, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

Re: Docket Number FDA-2010-N-0348

Dear Commissioner:

MedTech appreciates the opportunity to respond to the Food and Drug Administration's Preliminary Report and Recommendations of the 510(k) Working Group and Task Force on the Utilization of Science in Regulatory Decision Making.

MedTech is the hub of the Bio/Med industry in Upstate New York. It is a very active association of pharmaceutical, biotech, and medical technology companies, their suppliers and service providers, and research universities. Since its founding in 2004, the association has grown to more than 95 member organizations, which are listed in Attachment A. MedTech boosts the growth and prosperity of bioscience and medical technology companies by connecting them for collaboration, offering educational programs, sharing news and information, and advocating for the industry with government and community leaders. More information about MedTech and its member organizations can be found at www.medtech.org.

Background

The FDA has prepared this preliminary report as part of a two-pronged, comprehensive assessment of the 510(k) process. The other, important, component of this assessment is the ongoing independent study by the Institute of Medicine (IOM), expected to conclude mid-2011. MedTech believes that comprehensive reform requires consideration of both components of the assessment and requests that FDA thoroughly evaluate the IOM findings prior to implementation of any major change to the existing 510(k) process. We understand that FDA intends to work with IOM and consult with IOM in reviewing the comments FDA receives.

Comments

We provide here our comments to the preliminary reports for your consideration in improving the 510(k) process. MedTech members support the initiative to improve predictability of 510(k) reviews and data requirements. We agree that CDRH should provide industry with clearer evidentiary expectations that have consistent application. The result of clarified expectations and more detail in guidance to industry should have the very positive result of 510k submissions that are more complete and able to be reviewed and processed by the FDA efficiently. Along these lines, MedTech agrees with FDA's proposal to develop guidance and standard procedures for development and assignment

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FDA-2010-N-0348

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of product codes, a component of the classification process that is important and currently not consistently applied or transparent to industry.

Volume I: 510(k) Working Group

1. A Rational, Well-Defined and Consistently Interpreted Review Standard

> **"Same Intended Use"**

MedTech agrees that the definition of "substantial equivalence" should be clarified through guidance and that, as currently used, the terms "intended use" and 'indications for use" are confusing and not applied consistently by industry or the FDA. These terms are currently used to distinguish between two very different concepts – the "intended use" of a device which is a factor in determining "substantial equivalence" and the "indications for use" which describes in detail the use environment, methods, or circumstances. As acknowledged by the FDA 510(k) Working Group, there are concerns with simply blending the terms "intended use" and "indications for use". MedTech believes that, in an effort to combine the terms, further confusion may result; particularly with regards to manufacturer's ability to modify labeling regarding an "indication for use" without triggering a change to the "intended use." Thus, we strongly disagree with the recommendation to consolidate the terms "intended use" and "indications for use." MedTech suggests that the FDA clarify these two terms, as historically and currently used, in a guidance document or through regulation.

Additionally, MedTech strongly disagrees with the specific recommendation to allow FDA reviewers to determine the "intended use" of a particular device. It is our belief that the manufacturer of the product is in the best position to evaluate the use and labeling of the device, and also to appropriately monitor the changes to the use and labeling of the device, in order to remain compliant with regulatory obligations. If FDA implements this proposal to permit FDA reviewers to determine the "intended use" of a device, MedTech requests that FDA establish, through administrative rulemaking, a process that would address the following:

a. The process used by FDA to gather evidence to determine that an off-label use is the primary intended use. MedTech recommends that, at a minimum, the usage of the predicate device, coupled with testimony from medical professionals would be necessary to determine whether off-label is the primary usage.
b. A process that allows a manufacturer to appeal the decision to include an 'off-label' use as a primary 'intended use'.
c. An implementation plan that addresses how products currently on the market are impacted by subsequent determinations regarding "intended use" for predicate devices.

MedTech believes that the manufacturer promotional efforts are the appropriate approach to determining whether an "intended use" is off-label. MedTech requests that the FDA review its authority in this area given the long-standing delineation between FDA approval and state regulated practice of medicine issues.

> **Rescission Authority**

MedTech agrees that products that are dangerous to health should be examined and controlled or removed from the market. The scope of this authority, however, should be narrowly defined and rescission of a 510(k) clearance should be exercised only under limited circumstances. Furthermore, a reasonable period of time should be provided to the manufacturer to remedy any device defects, potential hazards, patient risks, or other specific health/safety concerns identified prior to pursuit of 510(k) rescission by FDA. Additionally, rescission authority should not be applied retroactively.

additional arguments necessary to satisfy safety and effectiveness concerns without necessarily having to undertake the clinical studies necessary for a PMA.

Moreover, reforms to the de novo process could serve to solidify the de novo process as a meaningful procedural mechanism to essentially appeal adverse (NSE) 510(k) determinations. The need for this "appeal" mechanism is especially important given the data presented in the CDRH Preliminary Internal Evaluations (Vol. 1) suggesting substantial internal lack of consistency in CDRH's decision making (see p. 52). We would encourage FDA to delineate a meaningful mechanism, conceivably through the revised de novo process, whereby manufacturers could appeal 510(k) decisions.

A second concern with the de novo process is that manufacturers must submit a 510(k) before they may request reclassification under 513(f)(2). The statutory language (quoted above) indicates that submission of a 510(k) is a prerequisite to submitting a de novo request. In the case of technological advances, given this constraint, the only option for manufacturers is to use "split" or "multiple" predicates, since currently manufacturers may not proceed directly to de novo review. Rather than explicitly disallowing the use of "split" predicates, FDA should create guidance similar to that it intends to draft for "multiple" predicates, explaining the circumstances in which use of more than one predicate is appropriate.

CDRH recognizes that there are instances where it is clear that a device has new intended uses or different technological characteristics that raise questions of safety and effectiveness, and that it is an inappropriate allocation of resources to undertake a lengthy 510(k) review (see Vol. I, p. 65). In fact, CDRH discusses the legislative history for passage of 513(f)(2), noting that the intent of introducing the de novo process was, in part, to "prevent attempts to fit devices into the 510(k) framework that are not suited to a predicate comparison: it would allow FDA to 'avoid time and resources consuming [sic] substantial equivalence determinations that rely on remote predicates.'" (Vol. 1, p. 63-64). To give effect to this legislative intent, CDRH should determine and specify the circumstances in which a quick NSE determination would likely be appropriate (p. 65). This could be accomplished by providing additional guidance through the 513(g) process whereby "pre-submission engagement between submitters and review staff" could reduce time spent inappropriately in the 510(k) process. As noted in the comments (p.104), FDA should "establish a mechanism for early collaboration with the manufacturer and an expedited process for initiating review of de novo requests" and "issue additional guidance on the threshold for clearing a device through the de novo process." MedTech strongly agrees with this initiative and encourages the FDA to consider all of these issues when revising the de novo process.

2. Well-informed Decision Making

> Unreported Device Modifications

MedTech members agree with FDA's proposal to revise existing guidance to reconcile the language in the 510(k) flowchart with the statutory language in Section 513(i) of the FDCA (See Volume I, pg. 57). And, MedTech supports FDA's efforts to revise existing guidance to clarify what types of modifications do or do not warrant submission of a new 510(k).

MedTech members are adamantly opposed to FDA's proposal to require manufacturers to provide regular, periodic updates regarding device modifications and the manufacturer's decision to not submit a new 510(k). FDA conceded, during the August 31st webcast, that there are a relatively small number of cases where the FDA finds, subsequently, that a manufacturer's decision to *not* submit a new 510(k) was incorrect. We believe that concerns regarding the decision making process manufacturer's use to assess whether a modification requires a new 510(k) could be, and are appropriately, addressed through clarification to the guidance on device modifications. MedTech

Although MedTech agrees that FDA needs to develop guidance on when a predicate device can no longer be used in subsequent applications, MedTech is concerned by FDA's proposal to have post-clearance authority to remove a device from the pool of available predicates. In order to ensure clarity, we request that FDA clearly prepare guidelines that will identify whether the device at issue is removed from the market, simply no longer available as a predicate but still available on the market, and, in the later circumstance, whether the devices that relied upon the rescinded device are impacted. In that vein, MedTech strong believes that before devices that relied upon the rescinded predicate are formally impacted, the FDA provide an opportunity for those manufacturers to defend their own devices and address the FDA's concerns in a formal regulatory proceeding. In the case of predicates that have been removed from the market (but not victim to 510(k) rescission), the use of these predicates should not be strictly prohibited so long as the safety and effectiveness of the device can be demonstrated. The FDA could allow the use of these predicates as "supplemental evidence of safety and effectiveness" in addition to demonstrating equivalence to a more current/FDA-recognized predicate. Regardless, the FDA should make clear efforts to provide industry with an updated list of devices that are "available" or permissible to be used as predicate devices.

In summary, MedTech believes that this issue is important enough to require that the FDA issue a regulation regarding their ability to rescind a 510(k) status of a device. This regulatory authority should be detailed enough to provide the scope, grounds, and appropriate procedures FDA will use in the rescission process and must include an opportunity for administrative appeal and review.

> **Use of "Split Predicates" and "Multiple Predicates"**

The 510(k) Working Group recommends disallowing the use of "split predicates." MedTech agrees that, in limited circumstances, the use of predicates with vastly difference technologies simply as a way to obtain that predicate's "intended use" may be inappropriate. MedTech recommends that rather than disallowing the use of "split predicates" entirely, FDA undertake the task of clearly defining circumstances and setting guidelines for the use of "multiple predicates" and "split predicates." This clarification will assist both FDA reviewers *and* manufacturers in the preparation of submissions. Additionally, we suggest that these guidelines contemplate an appeal or reconsideration process for unusual circumstances so that manufacturers facing the need to use "split predicates" for a device have the opportunity to fully explain and justify that position to the FDA.

Reform of the De Novo Process

MedTech understands, from FDA"s August 31, 2010 webcast on these preliminary reports, that one option is to use the de novo process more effectively to handle the unique circumstance of accelerated technological innovation that makes reliance upon only one existing predicate difficult or impossible. MedTech agrees with the proposal to reform the de novo classification to allow a well defined, predictable regulatory pathway for eligible devices for which there is no clear predicate. We request that FDA also consider the unique circumstances where "multiple" and/or "split" predicates may be justifiable and adequately rationalized by a manufacturer and include mechanisms in the reformed de novo process to address these circumstances.

One existing problem with the de novo process (that many MedTech members have experienced firsthand) is that the committee or team reviewing the 510(k) is also the group that will review any de novo classification requests under 513(f)(2). In fact, according to the FDA's February 19, 1998 513(f)(2) guidance document, "if, while reviewing the 510(k), the division determines that the device is not a likely candidate for Evaluation of Automatic Class III Designation, the NSE letter should indicate that FDA believes premarket approval will be necessary prior to marketing the device." In practice, this results in the 510(k) review team contemplating 513(f)(2) classification *during* the 510(k) review. However, for the statutory language of 513(f)(2) to have any real meaning, the de novo process must be an independent, impartial consideration of reclassification based on what would be a revised submission to the FDA, whereby the manufacturer would be afforded an opportunity to make any

thinks the current FDA enforcement and compliance tools are more than sufficient to handle the rare situation when the decision to not submit a new 510(k) was incorrect. Specifically,

1. FDA already has authority to review a manufacturer's analysis regarding device modifications in targeted, general, or for-cause inspections.
2. Manufacturers are already obligated, whether explicitly in a device specific guidance or practically through requests by FDA reviewers, to provide information regarding device modifications. In fact, where a modification has triggered a new 510(k), the majority of manufacturers use their existing cleared device as a predicate and provide a description of the modifications as part of the substantial equivalence discussion. MedTech recommends that FDA clarify that device modifications be detailed in subsequent 510(k) submissions and provide additional guidance on how such information should be conveyed within the 510(k) submission.

MedTech is concerned that the FDA will not have the appropriate resources to analyze and process these proposed modification reports, thereby creating an additional reporting burden on industry with little value to FDA or the public. MedTech strongly disagrees with the FDA's proposal to force all manufacturers, the vast majority of which are currently applying the regulatory requirements for analysis of device modification correctly, to incur significant time and cost in reporting device modifications to the FDA.

MedTech requests that FDA directly clarify whether a proposed modification to a device will need to be approved by the FDA in this new process and whether the FDA will have the ability to intervene in a manufacturer's planned or recently implemented modification.

Alternatively, a less burdensome approach could be for the manufacturer to maintain the 510(k) file, including non-substantial changes, on a periodic basis (i.e. annually) (similar to EU class II devices) and have the file available upon request during facility audits.

If the FDA proceeds with this unnecessary and undesirable reporting requirement, against industry recommendations, MedTech requests that:

- FDA further justify what it intends to do with the reports received and how modification reports will be utilized (for example, will modification reports be available to the public?).
- FDA consider the effect that the modification reports have on the ability of other manufacturers to use that device as a predicate. Will devices relying upon the modified device be required to consider and address all modifications when using that device as a predicate?
- If modification reporting is implemented, the FDA not make such modification reports available to the public.
- FDA consider requiring modification reports only once every 5 years, similar to EU class III devices
- FDA provide clear, prospective guidance on what types of modifications are required in such reports (i.e. non-significant changes that do not require a new 510(k) or a letter to file).

Finally, MedTech is very concerned about the effect that reporting of changes will have on a manufacturer's ability to be competitive in the market. Many manufacturers modify devices to address customer preferences (such as color, shape, and certain functionalities). The ability to make these minor adjustments quickly provides a competitive advantage in the marketplace.

> **Quality of Submissions**

The 510(k) Working Group recommended that a new requirement for an "assurance case" be required in all 510(k) submissions. MedTech requests that the FDA reconsider this recommendation as applicable to all 510(k)s. We understand that "assurance case" methods are used in other industries, and in fact have been required by the FDA for specific devices like infusion pumps. Although this detailed framework may be appropriate for some devices, perhaps like those in the yet-to-be-defined Class IIb category, MedTech disagrees that "assurance case" reports should be required in all 510(k)s. What FDA does not make clear in the preliminary report is that the "assurance case" reports, in fact, will require that additional evidence that is not currently required (such as human factors analyses) be included in the submission. MedTech recommends that FDA reserve the use of "assurance case" reports for limited circumstances and that FDA do so through device specific guidance rather than for an entire category of device.

The 510(k) Working Group also recommends that detailed photographs and schematics of the device be provided as part of the clearance process. The FDA's preliminary report has done little to assure manufacturers of the ability of the FDA to protect a manufacturer's intellectual property. MedTech's members are extremely opposed to the FDA's suggestion that such photos or schematics be made available to the public in a searchable database. The industry duly notes FDA's stated sensitivity to the proprietary nature of this information, but feels strongly that the FDA fails to completely appreciate the criticality of this information in the device industry. Medical devices have a unique nature compared to drugs and biologics. Many devices rely upon trade secrets or other non-patented methods and mechanisms to remain competitive and profitable. This industry does not receive the same level of patent protection as the drug industry, and therefore the potential damage resulting from inadvertent or intentional disclosure by the FDA is extraordinary.

Given that the potential for harm to the device industry is so great, MedTech requests further explanation from the FDA on the benefit that could be gained by requiring that this information be provided. It is our understanding that, where such information would not be harmful to the manufacturer, most manufacturers do in fact provide this information, both to the FDA and in the public domain (such as company websites, etc). The burden, in the existing 510(k) process, is on the manufacturer to explain the device functionality and provide the appropriate and necessary comparisons to predicate devices. MedTech discourages FDA from a system encouraging individual 510(k) reviewers to independently evaluate the product based upon schematics and photographs.

MedTech encourages the FDA to re-visit this issue and more carefully justify the minimal benefits of requiring this information compared to the massive damages that could result across the industry.

FDA also proposes to require manufacturers to keep one unit of the device available for the FDA to reference with regard to regulatory submissions relating to that device *or* to assist reviews in which the device is cited as a predicate. Although many MedTech members support the concept of FDA review of a physical device as part of the 510(k) review process, they disagree with the requirement to retain these devices for a longer period. Many of MedTech's members have identified the extensive burden this requirement may cause. Some devices are quite large and very expensive. Requiring the manufacturer to sequester one device could unduly burden the manufacturer. MedTech has serious concerns about FDA's implication that these reserved devices would be used during evaluation of a later device submission citing the reserved device as a predicate. Manufacturers also worry what implications this requirement may have for devices that work alone or in conjunction with other devices. Will manufacturers be required to retain the second device for connectivity analysis?

Before FDA proceeds with this requirement to retain devices, MedTech urges that FDA consider the broader implications, including the following questions:

- What obligation does the manufacturer have to its competitors as a predicate device?
- Will FDA require the reserved device manufacturer to allow access to the device manufacturer citing the predicate?
- Will FDA require these devices to be reserved if the manufacturer has made a modification, released a new model, or discontinued the device?

> **Incomplete Information**

MedTech disagrees with the FDA's proposal to require manufacturers provide all information known to the manufacturer about the device, including its own tests or studies that it has participated in, even if they failed or were unsuccessful. MedTech members believe that most failed tests are conducted again, with corrective measures taken or re-engineering of the device. If FDA requires submission of tests during the device development period, MedTech fears the result would be an unintentional incentive for manufacturers to *not* thoroughly test devices or apply rigorous failure standards to testing. The resulting impact on device quality and design is unknown, but could be substantial. MedTech members believe that quality information provided to the FDA is important, but requests that FDA's evaluation of that information be focused on the information provided by manufacturers rather than requiring non-beneficial information be submitted.

MedTech also disagrees that manufacturers should be required to provide a full bibliography and summary of scientific information regarding the safety and effectiveness of a device. The burden and cost involved in providing this information is substantial compared to the usefulness of the information expected. And, although MedTech appreciates FDA's public health function, MedTech requests that FDA thoroughly revisit the statutory authority regarding the 510(k) process, as it does not require a thorough evaluation of safety and effectiveness for each device. A fuller discussion of this point follows below.

> **Type and Level of Evidence Needed**

The 510(k) Working Group recommends that FDA use existing administrative tools to distinguish between lower-risk Class II devices and more risky Class II devices (to be called Class IIb devices) that will require a higher level of evidence to justify clearance. MedTech encourages FDA to use current administrative tools, such as guidance documents and CFR descriptions, to implement certain beneficial 510(k) Working Group recommendations for specific devices, rather than establish an entirely new classification for a category of devices--"Class IIb" devices. Although the FDA has characterized this expansion as a "clarification" of existing authority, MedTech believes this is merely semantics. MedTech argues that the FDA may not implement a new classification category, as proposed, without specific expansion of and amendment to the classification structure by Congress. MedTech believes statutory changes are required and appropriate to implement the proposed changes and does not recommend FDA by-pass them in order to simply implement changes quickly. Although FDA has made clear its intent to implement this classification change rapidly, MedTech specifically requests that FDA wait for the IOM study results and also take into account the failure of last year's GAO report to recommend such a classification change.

The legislative history surrounding the 510(k) process indicates that the term "substantially equivalent" is not intended to be so narrow as to refer only to devices that are identical to marketed devices nor so broad as to refer to devices which are intended to be used for the same purposes as marketed products. The Congressional Committee believed that the "term should be construed narrowly where necessary to assure the safety and effectiveness of a device but not so narrowly where differences between a new device and a marketed device do not relate to safety and effectiveness." Thus, differences between "new" and marketed devices in materials, design, or energy source, for example, would have a bearing on the adequacy of information as to a new device's safety and effectiveness, and such devices should be automatically classified into class III. On the other hand, copies of devices marketed prior to enactment, or devices whose variations are

immaterial to safety and effectiveness would not necessarily fall under the automatic classification scheme." (Vol. 1, p. 24).

FDA is concerned with the quality of predicates, and devices ability to "piggy back" on other devices (Vol. I, p. 57). However, this was precisely Congress' intent. FDA should improve its control over devices which it deems acceptable/unacceptable as predicates as MedTech has discussed above.

To the extent FDA imposes new requirements in the 510(k) process that approximates the requirements of PMA, such an action goes against legislative intent and statutory requirements. The 510(k) process was never intended to establish safety and effectiveness per se, but safety and effectiveness compared to another legally marketed device.

MedTech members argue that FDA's failure to confront the statutory limitations of the 510(k) program directly, but rather to sub-classify and essentially create a fourth classification with new obligations on industry, may actually cause further damage to the 510(k) program – increasing confusion and undermining legitimacy of the process. This approach is likely to cause significant additional confusion. For example, if FDA imposes a requirement for post market surveillance to address a safety concern, should not that device be properly classified as Class III and not as Class IIb? Would the post-market surveillance requirement also apply to all devices in this class?

In carefully reviewing the proposed Class IIb requirements, MedTech concludes that the FDA is in actuality requiring a level of evidence required by statute for Class III devices (which have not had their safety and effectiveness substantiated and are not eligible for the 510(k) program). This level of evidence is simply not a statutory requirement for 510(k) devices. The type of evidence identified by FDA for this new Class IIb include "clinical information, manufacturing information, or, potentially additional evaluation in the post-market setting." MedTech is concerned that this sub-classification will lead to an additional burden on manufacturers to conduct pre-approval human studies where not currently required or necessary.

If FDA persists in implementing this classification change without authority from Congress, MedTech requests further explanation from the FDA regarding the distinction between Class IIb and Class III. FDA might consider the Global Harmonization Task Force framework or the classification system used by the European Union as an example of a four-tiered classification system, in part to more closely align with International Standards thereby reducing the burden on the manufacturer for meeting multiple country standards. MedTech firmly believes that FDA should not implement this classification amendment without regular and substantive input from industry.

Industry is concerned that FDA cannot fully appreciate all of the market forces and commercial issues that would be significantly impacted by this classification change. For example, devices identified by FDA as Class IIb will be considered a higher risk than Class IIa – with the resulting product liability risks, but without the protections afforded Class III devices approved through the PMA process in *Riegel*. MedTech requests that FDA convene a working group with industry representation, specifically with small manufacturer representation, to fully address these industry issues in the amendment to the classification structure.

Additionally, there currently are Class III medical devices that are permitted to utilize the 510(k) process for review or clearance of modifications (e.g. dialysis catheters). MedTech members that are manufacturers of these devices are concerned that the additional category and requirements for a Class IIb device will limit this existing process for low-risk Class III devices and make the regulatory process for such low-risk, commodity devices overly burdensome.

> **Clinical Information**

More fundamentally, we question the FDA's position that clinical evidence is needed to establish safety and effectiveness but that those devices are still within the same risk classification and not "up-classified" into Class III. The need for a clinical evaluation of the device fundamentally calls into question its ability to be considered substantially equivalent to a predicate device. Placement in Class IIb will, necessarily, presume that there are suitable predicate devices whose clinical performance is understood. Safety and effectiveness is invoked in the context of a 510(k) only to establish that a device is "as safe and effective as a legally marketed device," not that it is "safe and effective" in absolute terms. While the FDA may request "clinical or scientific data" in a substantial equivalence determination, Section 513(i)(1)(D) states, "Whenever [FDA] requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, [FDA] shall only request information that is necessary to making substantial equivalence determinations. In making such requests, [FDA] shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly."

In other words, any data requested by the FDA in a 510(k) submission should rightfully be aimed at establishing substantial equivalence, not safety and effectiveness in absolute terms. Even the Supreme Court has recognized that there is a significant distinction between the 510(k) substantial equivalence and PMA process with respect to evidentiary burden. (See for example, Medtronic, Buckman, and Riegel cases). These cases note that 510(k) is "by no means comparable to the PMA process" (Medtronic) and that the "510(k) process lacks the PMA review's rigor" (Buckman). The resulting distinction has significant product liability and contractual outcomes that FDA should seriously consider before modeling the evidentiary requirements in the 510(k) process after the PMA requirement. Specifically, if FDA requires clinical information similar to a PMA, FDA should seek to amend the statutory and regulatory distinctions in such a way that a 510(k) submission would afford comparable product liability protections to a PMA.

MedTech members agree that the FDA should provide clarity with regard to the level of clinical data that would be appropriate to support 510(k) product clearances. MedTech requests that the FDA clarify what is intended by its use of the term "clinical data." Does this mean FDA will require that new studies be conducted? Or does this mean that a 510(k) submission can meet the burden of including "clinical data" through a thorough clinical literature review and discussion?

> **Post Market Information**

MedTech is concerned by FDA's proposal to impose requirements for post-market surveillance or to condition clearance upon post-market evaluation results. FDA has inadequately described how requiring specific post market clinical studies will provide any additional information beyond what FDA already has access to – including MDRs, corrective action reporting, and, more recently, total life cycle reports. MedTech believes that imposition of additional post-market surveillance, in light of the information already provided to the FDA, will be burdensome and costly with minimal benefit to public health.

The FDA's recommendation to use "real-world' data in evaluating a premarket notification for a device is confusing. It is unclear who the FDA expects to compile this information and the weight that will be given to information that may not be compiled by the manufacturer of the device. MedTech requests that the FDA clarify how the use of "real-world" device use data will be compiled (particularly when the data is generated without involvement or awareness of the manufacturer) and how the FDA intends to use this information during the 510(k) review process. MedTech is concerned that application of this proposal to the device under review would result in significantly more IDE submissions and extend the approval times. MedTech also requests that FDA directly address the challenges of obtaining informed consent when providing guidance on the collection and use of such anonymized "real-world" data. Finally, MedTech requests that the FDA clarify whether this data will

be available to device manufacturers (in the public database or otherwise) for use in analyzing predicate devices and developing post-market surveillance measures.

> **Manufacturing Process Information**

Although MedTech generally agrees that the FDA should consider including pre-clearance inspections as part of the 510(k) review process for manufacturers with a poor GMP compliance history or for manufacturers with recent compliance issues that should be corrected before new devices are introduced, MedTech requests that the FDA further consider whether non-compliance with GMPs actually present serious risks to human health for products classified into a class that requires premarket notification (510(k)) prior to introduction into the commercial market. Such inspections currently fall under FDA's statutory authority.

MedTech objects to standard pre-clearance inspections for all premarket notification applications. This would result in delays to market with minimal, if any, benefit to public health. MedTech requests that the FDA release publicly more data regarding the need for such pre-clearance inspections and the basis upon which FDA relies to propose this recommendation. To require pre-clearance inspections for any 510(k) submission calls into question whether that device should truly be classified as Class II.

> **510(k) Databases**

MedTech agrees with FDA's proposal to update the 510(k) database to include more information and better demonstrate how related devices and subsequent devices are linked. In addition to the features and updates FDA has proposed, MedTech suggests FDA consider including information on when a device is transferred and detailed information on which devices are covered by a specific 510(k). MedTech agrees that the FDA should have the ability to update the 510(k) database to properly reflect commercial transfers ownership of 510(k)s in the market. FDA should have a process in place for updating product listings so manufacturers can provide a more accurate list of 510(k)s for their chosen predicate device or for their product lines (as may be needed in corporate acquisitions or in 510(k) substantial equivalence discussions).

Our members request clarification on whether the FDA's proposal to require manufacturers to submit final labeling means that the FDA will be reviewing and approving such labeling, or simply that the FDA will be collecting and making publicly available such labeling. FDA should also clarify which types of labeling will be required to be submitted (user manuals, direct device labeling, etc). MedTech is concerned that FDA's proposal for updated labeling to be submitted will encroach upon a manufacturer's ability to engage in constitutionally protected commercial speech, particularly since many changes to labeling are for advertising and marketing purposes and not for regulatory or device change purposes.

Furthermore, the FDA should consider whether the implementation of this proposal would infringe on the Federal Trade Commission's (FTC) regulation of the advertising of most medical devices under §§12-15 of the Federal Trade Commission Act which prohibits misleading or false advertising. Given FDA's limited authority over the advertising of most medical devices, MedTech requests the FDA clarify whether FDA intends to require such "advertising" or "marketing-related" labeling changes be submitted for review by FDA in order to maintain the database as current. In such case, MedTech recommends the FDA provide clarification on what types of changes would be required to be submitted and provide an explanation on the distinction between the materials FDA requests and those regulated by the FTC.

Again, MedTech members are extremely concerned with the information FDA proposes to make available in the 510(k) database. FDA should ensure that all manufacturer trade secrets are protected and that there is a mechanism available for manufacturers to ensure against inappropriate disclosure, request changes, and for retraction of information made public.

3. **Continuous Quality Assurance**

We applaud efforts to enhance the consistency of decision making within the FDA by improving training, recruitment, etc. of the review staff. Our comments on the Task Force on the Utilization of Science in Regulatory Decision Making follow. However, MedTech requests further clarification from FDA on the model to be used to "periodically audit 510(k) review decisions." Specifically, what are the potential follow-up actions to the proposed 510(k) audits? Could a 510(k) clearance retroactively be withdrawn? Device manufacturers request specific guidance on how these audits will impact their reliance on clearance decisions previously made and that FDA provide an administrative appeal process that includes the manufacturer's ability to present data regarding the device's performance and safety since being cleared for market.

Volume II: Task Force on Utilization of Science in Regulatory Decision Making

1. **Enhancing CDRH's Scientific Knowledge Base**

    1. Clarification of least burdensome should result from some of the suggested changes.

    2. In improving the design and performance of clinical trials and IDE decision making, FDA should make the IDE decisions binding on the agency.

    3. FDA should review the clinical requirements in all current guidance documents to assure there are accepted scientific methodologies for conducting and evaluating the studies (example: comparative features analysis for digital mammography).

    4. When tapping scientific expertise will FDA be required to follow the recommendations of the experts?

    5. MedTech supports the proposal for FDA to be involved in establishment and adoption of domestic and international consensus standards.

2. Applying a Predictable Approach to Determine the Appropriate Response to New Science

MedTech welcomes the FDA's initiative for creating a framework to respond to new scientific information. Besides input from FDA staff and management, the process should allow for input from industry, academia and the medical profession.

In light of new science where further information about a particular device-related event is required to understand the extent of a potential public health issue, clarification is needed on how and under what circumstances FDA will mandate additional post-market surveillance studies for devices already on the market. Considering the costs and resources associated with the planning and execution of post-market studies, FDA should consider how quickly manufacturers will be required to respond to such requirements.

3. Promptly Communicating Current or Evolving Thinking to All Affected Parties

MedTech welcomes the Task Force's recommendation to promptly communicate current or evolving thinking. We believe this can be done under the constructs of the current administrative protocols at FDA. Specifically

    1. MedTech welcomes the recommendation for FDA to allow external constituencies (industry, academia, etc.) to provide draft guidance documents for their consideration. Many of these constituencies have the scientific and technical expertise required to provide a workable draft guidance document.

2. Similar to a panel meeting, FDA should consider engaging panels for creation and review of guidance documents relating to specific technology requirements and clinical studies for those technologies.

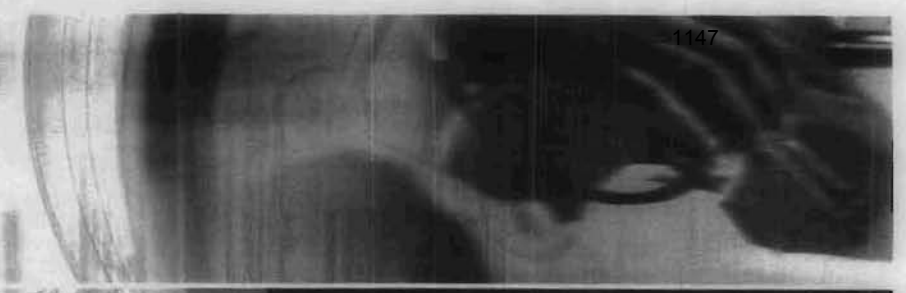
Again, MedTech appreciates the FDA's consideration of these comments to the Preliminary Report and Recommendations of the 510(k) Working Group and Task Force on the Utilization of Science in Regulatory Decision Making. MedTech's unique position as the primary voice for medical device manufacturers in New York demands special consideration of these comments. The medical device industry continues to be an extremely important industry in New York and MedTech members look forward to working with the FDA to effectuate positive changes to the existing 510(k) framework.

Sincerely,

Heather Erickson

Heather Erickson
President, MedTech Association

MedTech



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Member Organizations

MedTech's mission is to develop the relationships, tools, and programs that enable Upstate New York companies to bring tomorrow's medical solutions to the healthcare marketplace.

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Bio-Optronics
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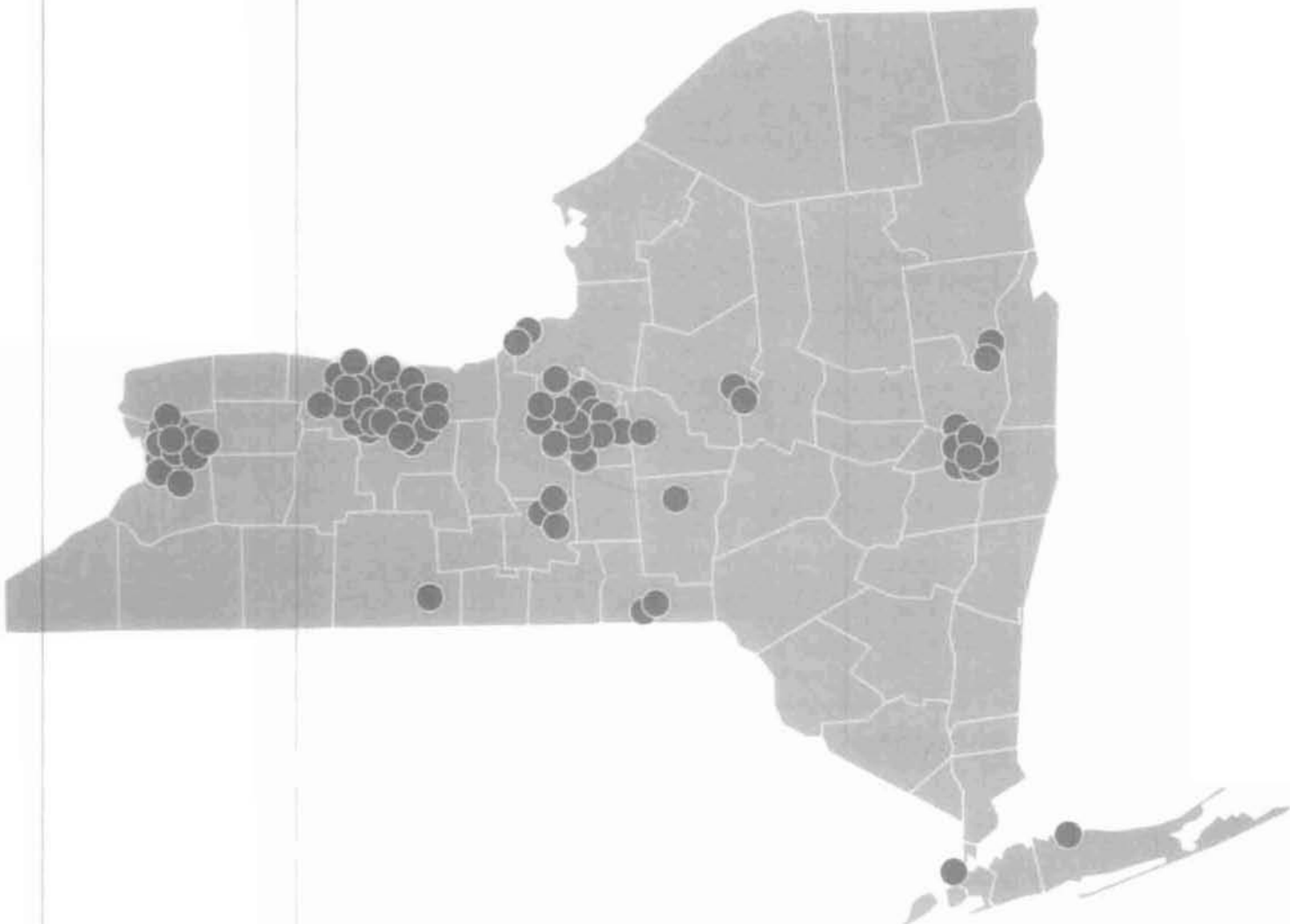
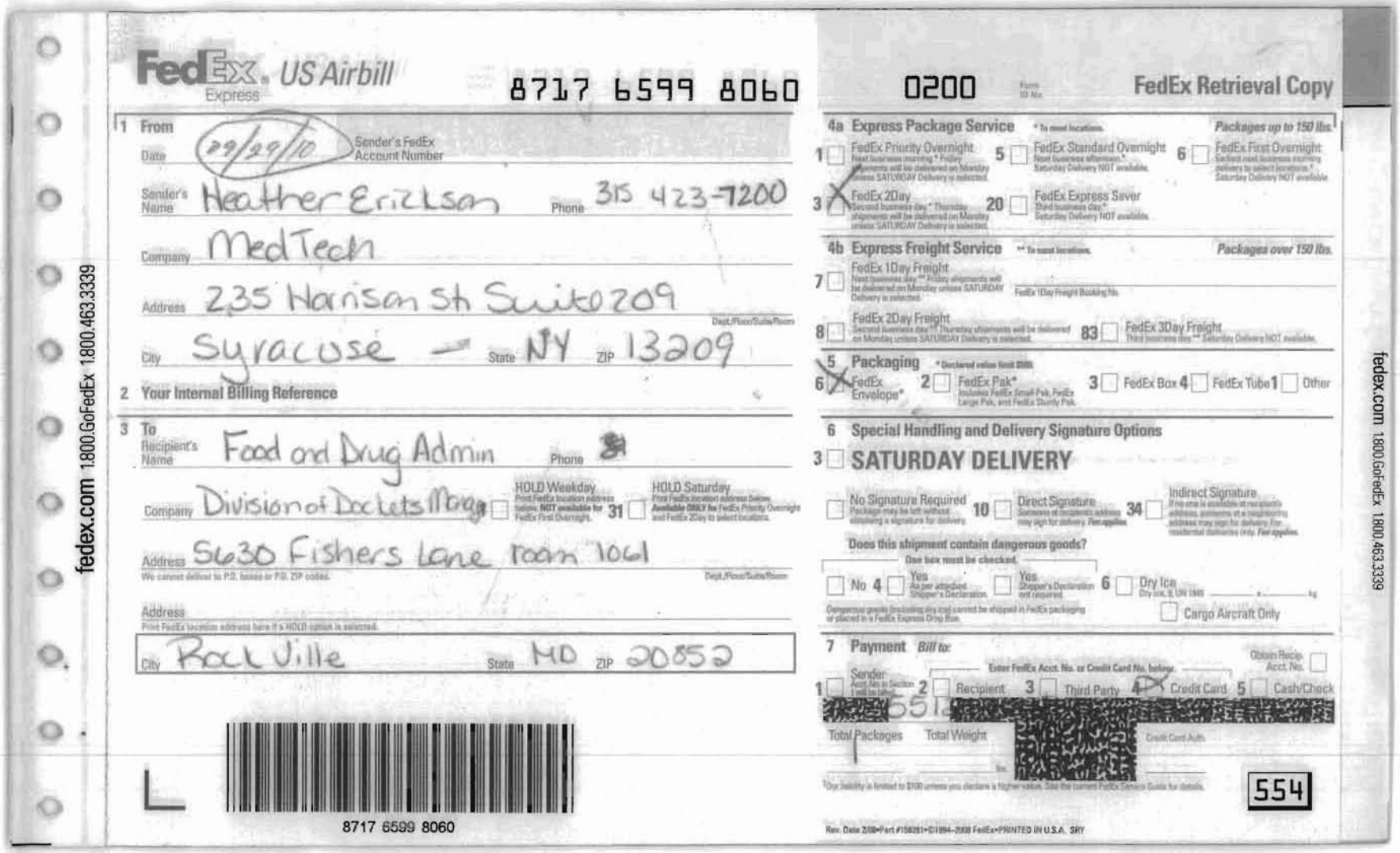


MedTech

The MedTech community currently includes 92 member organizations across New York State. MedTech Association, Inc. is a not-for-profit regional trade association comprised of Upstate New York technology manufacturers, research institutions, allied professional services firms and economic development organizations with shared interests in collaboratively developing technologies, products and services for the global bioscience and medical technology marketplace.



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4b Express Freight Service ** To most locations. Packages over 150 lbs.
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8 FedEx 2Day Freight — 83 FedEx 3Day Freight

5 Packaging * Declared value limit $500
6 X FedEx Envelope* — 2 FedEx Pak* — 3 FedEx Box — 4 FedEx Tube — 1 Other

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No Signature Required — 10 Direct Signature — 34 Indirect Signature

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The Orthopedic Surgical Manufacturers Association (OSMA) (Susan Krasny) – Comment (posted 11/02/10)

FDA-2010-N-0348-0068

October 1, 2010

2010 OCT -4 A 10: 14

Division of Dockets Management (HFA 305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2010-N-0348: Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations, and the Task Force Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability; Request for Comments

Dear Sir/Madam:

The Orthopedic Surgical Manufacturers Association (OSMA) appreciates the opportunity to submit comments on the proposed *510(k) Working Group Preliminary Report and Recommendations* as well as the *Task Force Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations*.

OSMA is a nonprofit organization whose membership consists solely of manufacturers of orthopedic surgical appliances, implants, instruments or equipment, and orthobiologics. Since its inception in 1954, OSMA has continued to actively participate in standards and regulatory guideline development, educate our membership on regulatory matters, provide regulatory professionals a forum to collaborate, communicate, cooperate, and interact with worldwide regulatory agencies and health care professionals on issues that lessen the regulatory burden and improve the application of device law. OSMA appreciates its collaborative relationship with the FDA and looks forward to working on recommended changes to the 510(k) program in the same way.

Benefit of the 510(k) Process

The orthopedic industry has a strong legacy of innovation in developing devices that relieve the pain of, and restore mobility to, patients of all ages from all walks of life, and the 510(k) process has been an essential part of this success story. The 510(k) pre-market review process is an effective component of a rigorous regulatory framework spanning the total product lifecycle of medical devices, and helps deliver important new orthopedic treatment options to patients in need. Approximately 90% of all medical devices are authorized to be marketed in the United States through the 510(k) process. OSMA is proud of its cost effective, life enhancing devices, and believes the current authorities of the 510(k) process allow it the flexibility and strength to respond appropriately to different categories of devices.

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FDA-2010-N-0348

Analysis of the 510(k) Process and FDA 510(k) Work Group and Task Force on Science Recommendations

OSMA fully supports the current 510(k) process, but recognizes the challenges facing the FDA and the 510(k) process. Additionally, OSMA appreciates that the 510(k) has evolved over time to meet changing needs and that currently proposed changes to the 510(k) regulations to improve the consistency and transparency in decision making could potentially benefit both patients and industry. However, it is imperative that any changes should be made cautiously and with the input of all stakeholders while maintaining the intent of this important process.

As outlined below in greater detail, OSMA supports many of the 510(k) Work Group and Task Force on Science recommendations, while also having many concerns. Across the board, OSMA believes that the potential cumulative effect of so many of these changes at once could disrupt the 510(k) review process and undermine patient access to necessary orthopedic medical devices.

OSMA recommends that the FDA adopt a phased approach to implementing the group of changes which ultimately move forward and that each change have a transition period. A phased approach with appropriate transition periods will ensure that the system is not overwhelmed and patients' access to enhanced orthopedic medical technologies is maintained. To that end, OSMA also appreciates the FDA's public comments that it will initially move forward only in areas which have consensus and that more controversial recommendations will be referred to the Institute of Medicine for further review.

Additionally, OSMA supports the 510(k) Work Group Recommendations regarding enhanced support for training and professional development for review staff, but believes that changes to the 510(k) process should only be implemented after all reviewers and stakeholders are appropriately trained. A key tool in educating stakeholders is the guidance process. OSMA fully supports the recommendation for more clear guidance and believes that further changes to the process should only be made after a system is in place for clearer and easily accessible guidance for the medical device industry.

Lastly, many of the 510(k) Work Group recommendations lack sufficient detail to allow OSMA to formulate an opinion or offer many comments. On certain issues, OSMA is supportive of the general concepts expressed in the reports but, in the absence of greater specificity, must reserve the right to oppose specific proposals until those detailed proposals are developed and made available for public comment. We appreciate FDA's public statements that it will release more specific details on its recommendations and allow the public time to comment before implementing changes to the 510(k) program.

OSMA has divided its comments into three sections: those we oppose, those we support with modifications and those we support.

OSMA **opposes** the following FDA recommendations:

- *FDA Recommendation: Establishment of formal Class IIb*
    - OSMA **does not** support the establishment of a formal Class IIb category, however,

we do support the for cause identification of a small, focused subset of higher-risk devices within Class II that would be determined on category by category basis, and open for public comment. This subset would be subject to additional requirements suitable for these higher risk devices.

- OSMA feels that as CDRH develops its guidance on this subset of devices, the focus should be on what evidence CDRH feels it needs to establish substantial equivalence and what special controls may be appropriate to mitigate the risk. The agency should take care not to head down a PMA-like path.
- As CDRH clarifies its evidentiary and submission requirements for this small, focused subset and becomes more comfortable with the agency's ability to mitigate the associated risk, OSMA also encourages CDRH to consider down-classifying some PMA devices that are not life-supporting or life-saving into this subset.
    - This small subset offers a rare opportunity to down-classify some Class III devices. The current classification of these devices in the United States may not accurately reflect the proven safety and efficacy of these products. OSMA believes that the subset of class II devices for which the agency can establish additional pre-market submission and post-market information requirements, could be a more appropriate classification for these devices.

- The following FDA recommendations that we **do not** support for all of Class II, but **do support for the small, focused subset** are:
    - CDRH should explore the feasibility of requiring each manufacturer to provide regular periodic updates to the Center listing any modifications made to its device without the submission of a new 510(k).
    - CDRH should develop guidance to provide greater clarity regarding what situations may warrant the submission of manufacturing process information as part of a 510(k), and include a discussion of such information as part of its "subset" guidance.
    - CDRH develop guidance to provide greater clarity regarding the circumstances in which it will request clinical data in support of a 510(k), and what type and level of clinical data are adequate to support clearance. CDRH should, within this guidance or through regulation, define the term "clinical data" to foster a common understanding among review staff and submitters about types of information that may constitute "clinical data.

- *FDA Recommendation. CDRH should explore possibility of explicitly disallowing the use of split predicates.*
    - We disagree that CDRH should eliminate use of "split predicates". While we acknowledge that this type of substantial equivalency comparison should receive additional scrutiny, a comparative risk analysis and/or additional design validation information may suffice to address remaining concerns.
    - Split predicates are appropriate to lower risk devices and are fundamental to prove Substantial Equivalence (determination of device classification; not clearance of the device)
    - Eliminating the use of "split predicates" could lead to an increase in unnecessary PMA and *de novo* filings. Although the use of split predicates may not be

appropriate in all cases, in many instances it provides a reasonable and practical approach to establishing substantial equivalence.

- Split predicates are vital to innovation and meeting public health needs, as many medical devices are modular in nature and made up of a combination of components.

- *FDA Recommendation: CDRH should explore pursuing a statutory amendment to section 513(i) (1) (E) of the Federal Food, Drug and Cosmetic Act to provide FDA with express authority to consider an off label use, in certain limited circumstances, when determining the "intended use" of the device under review through the 510(k) process*
  - OSMA cannot support such a statutory change and believes off-label use should not affect 510(k) clearance. Off-label use is at the physician's discretion, and should not be the burden of the manufacturer. However, it is OSMA's belief that FDA should adopt procedures that streamline companies' abilities to conduct clinical trials in the US and to look for alternatives to prospective controlled clinical trials for FDA authorization and approval of off-label uses.
  - Additionally, OSMA urges CDRH to use the tools currently available to the agency to curb *promotion* of off-label uses. OSMA also encourages CDRH to rely on its existing statutory authority to require statements in labeling that limit a device's use for off-label purposes, if the agency consults with the 510(k) sponsor and the following criteria are met: There is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device, and such use could cause harm. This provides a more flexible and less onerous alternative for CDRH to follow in protecting public health.

- *FDA Recommendation: CDRH should revise existing guidance to consolidate the concepts of "indication for use" and "intended use" into a single term "intended use," in order to reduce inconsistencies in their interpretation and application.*
  - OSMA believes that it is critical that the two concepts, "*indication for* use" and "*intended use,*" remain distinct and separate, as they clearly serve different purposes. Combining the two terms may constrain the meaning of intended use, and remove flexibility that the agency currently enjoys in determining what new uses should be regulated within the confines of section 510(k).
  - Confusion between the terms can be eliminated by developing clear definitions of each concept within the context of substantial equivalence through guidance, and training reviewers and industry on these definitions.

- *FDA Recommendation: The 510(k) Working Group further recommends that CDRH ... include a discussion of pre-clearance inspections as part of its "class IIb" guidance.*
  - OSMA does not support pre-clearance inspections for any Class II devices. Pre-clearance inspections have no relevance to determining significant equivalence.

- *FDA Recommendation. : The 510(k) Working Group recommends that CDRH consider issuing a regulation to define the scope, grounds, and appropriate procedures, including notice and an opportunity for a hearing, for the exercise of its authority to fully or partially rescind a 510(k) clearance. As part of this process the Center should also consider whether additional authority is needed.*

- OSMA opposes broad expansion of CDRH's rescission authority, but supports clarification of its rescission authority in the narrow case of fraud. We have significant concern that further expansion would jeopardize the legal marketing status of each device that had subsequently relied on the rescinded device as a predicate (i.e., the device would be misbranded), even if the concerns that prompted the rescission of the predicate device do not apply to the subsequent devices.
- FDA has numerous tools to remove violative devices from the market. If a device is considered unsafe because it is manufactured under noncompliant GMPs, is manufactured incorrectly, or the manufacturer has unlawfully changed the design without meeting the appropriate pre-market requirements, then that device should be appropriately dispositioned per FDA's current post-market authorities provided in the Act, including reclassification, recall, warning letters, and other enforcement actions. These conditions can be remedied, however, and should not be used as grounds for revoking the original 510(k) decision.

OSMA **supports, with modifications,** the following FDA recommendations:

- *FDA Recommendation: CDRH should explore the possibility of requiring each 510(k) submitter to provide as part of its 510(k) detailed photographs and schematics of the device under review, in order allow review staff to develop a better understanding of the device's key features.*
  - As stated in the CDRH Preliminary Internal Evaluation, many companies currently provide depictions of the device under review. However, it is important to note that at the time of 510(k) submission, the final version of the device may not be available or exist. It would be appropriate then that CDRH *request* a photograph or graphic depiction of the device under review as a means to aid the review process and not state it as a requirement. This request and the rationale for complying should be provided in the related guidance document.
  - It is important to acknowledge that the release of any confidential or proprietary information to the public must be done with the permission of the owner of the information, in this case, the sponsor of the 510(k) submission. CDRH must have processes in place that allow redaction of sponsor information before it is placed on a public website. Any photographs or graphic depictions of a device that would provide proprietary information to competitors, both domestic and outside the United States, therefore, should not be released to a publicly available website.
- *FDA Recommendation: The 510(k) Working Group recommends that CDRH explore greater use of its post-market authorities, and potentially seek greater authorities to require post-market surveillance studies as a condition of clearance for certain devices. If CDRH were to obtain broader authority to require condition□of□clearance studies, the Center should develop guidance identifying the circumstances under which such studies might be appropriate, and should include a discussion of such studies as part of its "class IIb" guidance.*
  - OSMA supports the use of FDA's current post-market authorities under section 522 of the Act and in the case of special controls under the section 513(a)(1)(B) of the Act. Under this authority FDA can require a manufacturer to conduct post-market surveillance for Class II and III devices.

- OSMA does not support recommendations for "broader authority" to require post-market surveillance as a condition of clearance for certain devices. As referenced above, FDA has the authority to require post-market surveillance of devices.

- *FDA Recommendation: CDRH should continue its ongoing effort to implement a unique device identification (UDI) system and consider, as part of this effort, the possibility of using "real□world" data (e.g., anonymized data on device use and outcomes pooled from electronic health record systems) as part of a pre-market submission for future 510(k)s.*
  - OSMA believes that the FDA UDI system requirements must be harmonized with global initiatives. The devices within a given UDI can vary widely in their performance, thus pooling data could tarnish the results for the entire class of devices. Consequently, firewalls must be put in place to prevent decisions on device types, based solely on UDI data.

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- *FDA Recommendation: CDRH should also explore 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, so that review staff could, as needed, examine the device hands on as part of the review of the device itself, or during future reviews in which the device in question is cited as a predicate*
  - OSMA believes that FDA should have the ability to request a unit only for devices under review with the understanding that the device is not used for performance testing or "type testing" and that the request does not delay the review time.
  - OSMA opposes any other use of a sample device, including its proposed use for future reviews of other company's products.
  - OSMA recommends that the FDA should return or destroy sample devices per the manufacturer's request.
  - It is important that FDA take into consideration the burden of storing such devices including the needs for refrigeration, large equipment, etc.

OSMA **supports** the following FDA Recommendations:

- CDRH should develop guidance and regulations regarding appropriate documentation of transfers of 510(k) ownership.
- CDRH should develop metrics to continuously assess the quality, consistency, and effectiveness of the 510(k) program, and also to measure the effect of any actions taken to improve the program. As part of this effort, the Center should consider how to make optimal use of existing internal data sources to help evaluate 510(k) program performance.

- CDRH should work to better characterize the root causes of existing challenges and trends in IDE decision making, including evaluating the quality of pre-submission interactions with industry and taking steps to enhance these interactions as necessary
- CDRH should assess and better characterize the major sources of challenge for Center staff in reviewing IDE's within the mandatory 30-day timeframe, and work to develop ways to mitigate identified challenges under the Center's existing authorities.
- CDRH should develop and make public a Standard Operating Procedure (SOP) that describes the process the Center will take to determine the appropriate response to new scientific information, based on the conceptual framework outlined above.
- CDRH should develop guidance and Standard Operating Procedures on the development and assignment of product codes
- CDRH should enhance training, professional development, and knowledge sharing among reviewers and managers, in order to support consistent, high quality 510(k) reviews CDRH should consider establishing a Center Science Council to serve as a cross-cutting oversight body that can facilitate knowledge-sharing across review branches, divisions, and offices.
- CDRH should clearly identify the characteristics that should be included in the concept of "intended use."
- CDRH should develop guidance and SOPs for the development of 510(k) summaries to assure they are accurate and include all required information identified in 21 CFR 807.92.
- The Center should consider developing a standardized electronic template for 510(k) summaries.
- CDRH should periodically audit 510(k) review decisions to assess adequacy, accuracy, and consistency. The ongoing implementation of iReview (described in Section 5.3.2 of the report), as part of the Center's FY 2010 Strategic Priorities, could assist with this effort by allowing CDRH to more efficiently search and analyze completed reviews. These audits should be overseen by the new Center Science Council, described above, which would also oversee the communication of lessons learned to review staff, as well as potential follow-up action
- CDRH should continue ongoing efforts to develop better data sources, methods, and tools for collecting and analyzing meaningful post-market information, consistent with the Center's FY 2010 Strategic Priorities.-

Again, many of the FDA recommendations are very general in nature and their impact will be very difficult to evaluate until specifics are provided. For this reason, we continue to urge the agency to provide further detail and additional comment periods on such details before taking any final action on those recommendations. In this regard, there are instances where OSMA may support the general concepts contained in the report but reserves the right to oppose or object to future detailed proposals of these general recommendations.

Conclusion

OSMA supports a healthy 510(k) system to continue to facilitate the availability of important orthopedic treatment options for American patients and physicians. As such, OSMA strongly recommends that the FDA move forward cautiously with any changes so as to not overwhelm the 510(k) process with too many simultaneous changes. There should be an appropriate phase-in or transition period for changes to allow time for the process to adapt and to allow patients continued access to important orthopedic medical technologies.

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OSMA appreciates the FDA's commitment to medical device innovation and hopes that the FDA will take these issues and recommendations under careful consideration, as they will have a great impact on patient access to important orthopedic technologies in future years. If you have any questions, please do not hesitate to contact me.

Sincerely,

Susan Krasny

Susan Krasny, Ph.D., RAC
President, OSMA

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BIOCOM (Joe Panetta) – Comment (posted 11/02/10)

FDA-2010-N-0348-0069

BIOCOM

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September 28, 2010

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

RE: BIOCOM Response to the "Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations, and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability for Comment." [Docket No. FDA-2010-N-0348]

To Whom It May Concern:

BIOCOM leads the advocacy efforts of the Southern California life science community with more than 550 dues paying members including biotechnology, medical device, and biofuel companies, universities and research institutions, as well as service providers. In our mission of providing feedback and communication between the industry and regulators, we are writing in response to the FDA's CDRH Internal 510(k) Working Group Report, Docket No. FDA-2010-N-0348, "Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability for Comment."

The proposed recommendations in the report include many changes to the 510(k) process that could impact the development and clearance of medical devices. There are areas where BIOCOM feels there is good alignment with the industry; for example, BIOCOM agrees with the approach CDRH's working group recommends for reforming the "De Novo" process. This includes steps to encourage pre-submission engagement between submitters and review staff, recommendations related to sound changes that streamline and clarify the expectations for de novo requests, what information should be submitted to determine eligibility for de novo classification, and recommendations which would establish baseline device-specific special controls. BIOCOM agrees the changes CDRH has proposed will help address inefficiencies and improve predictability.

Although the spirit of many of the proposed recommendations included in the CDRH Internal 510(k) Working Group Report appear to attempt to address what steps CDRH might take to improve the 510(k) program, a concern equally shared by the industry, BIOCOM has strong objections and concerns related to the following recommended changes:

FDA-2010-N-0348

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"Off-Label Use"

BIOCOM has strong objection to the working group's recommendation which suggests the FDA seek authority to consider an off-label use when determining the intended use of the device under review throughout the 510(k) process. This recommendation requires statutory change, which is outside of the FDA's purview. Further, the report cites tools the FDA already has at its disposal to limit off-label usage. The recommendation is focused on off label marketing, for which the FDA already has remedies that can be deployed if desired.

BIOCOM understands that in some cases, "true" intended use could raise issues to safety and effectiveness, however giving the FDA express authority to consider an off-label use would likely put a huge burden on the manufacturer, who would be required to provide safety and effectiveness data for uses which they do not intend their device to be used. BIOCOM recommends the FDA require manufacturers to identify potential uses that may occur outside of product labeling once a device has cleared and issue warnings if needed. Clear guidance related to the manufacturer's responsibility and liability in this area should be established.

Redefining and Clarifying "Substantial Equivalence"

BIOCOM agrees that insufficient clarity between different technological characteristics and different questions of safety and effectiveness has lead to confusion and delays in CDRH's review and decision making process. However, CDRH's recommendation to combine "indications for use" and "intended use" into a single term under 510(k) "substantial equivalence" is not sufficient and may lead to further confusion and add to delays. BIOCOM urges the FDA to develop guidance related to how the FDA defines "intended use" and whether the Agency requires a new device to have the identical intended use as one or more predicate devices to be substantially equivalent.

"Disallow Split Predicates"

BIOCOM objects to CDRH's recommendation to narrow the use of multiple predicates and explore explicitly disallowing the use of split predicates would likely have a negative impact on the development and innovative devices that are developed to enhance patient care. The use of combining proven solutions, multiple predicates and split predicates, has historically aided in innovative progress. BIOCOM believes it is appropriate for the FDA to develop guidance to identify situations in which a device should be disqualified as a predicate due to safety and efficacy concerns. Guidance should clarify circumstances under which CDRH would exercise their authority to remove a device from the market or preclude its use as a predicate.

"Rescission Authority"

BIOCOM strongly supports the FDA's responsibility in protecting the public through its regulation of medical devices. However, the Agency already has the authority to remove

unsafe devices from the marketplace through the Food and Drug Cosmetics Act. Rescission authority over 510(k) clearance gives the FDA overly broad power. CDRH's recommendation lacks legal protections that could be put in place for medical device companies whose products would face rescission. The public could be faced with the unintended consequences of having whole categories of safe and beneficial products removed temporarily from the marketplace, and manufacturers could be faced with the undue economic burden of having their already cleared devices forced off the market. More information is needed.

"New Class IIb"

The addition of a new class IIb device could add an unnecessary layer of confusion for manufacturers, companies and reviewers. As the FDA already may request clinical data, it does not appear the creation of a special category is warranted. If enacted, this recommendation needs more clarification. Would class II products currently on the market be grandfathered? Would the FDA have the authority to rescind clearance on a device already on the market? How is class IIb different from class III? A significant amount of additional information is needed.

"Requiring 510(k) Submitters to Provide all Scientific Information"

Development of medical devices differs significantly from that of drugs, and requiring submissions to include all scientific information known or that should be reasonably known to the submitter regarding the safety and/or effectiveness of the device under review would force manufacturers to over report non-relevant information, which could significantly increase the cost and time for manufacturers to prepare 510(k) submissions without contributing to the safety or effectiveness of the devices. This recommendation could subject a manufacturer to penalties if the FDA concludes that the information provided was incomplete or inaccurate. CDRH's report fails to describe how safety and effectiveness information would be used in determining if a device is substantially equivalent to its predicate. It fails to address what information is relevant and would force the industry to over-report scientific information or risk legal breach and could lead to an increase in the need for FDA involvement in trivial invalid investigations, resulting in a costly and unnecessary burden on FDA resources.

"Improvements to online 510(k) Database"

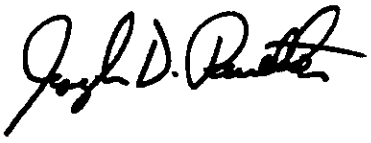
BIOCOM has significant concerns over CDRH's proposal to post publicly schematics and FDA review decisions on an online 510(k) database. Design schematics and photographs should not be readily accessible to external parties unless proprietary information and intellectual property (IP) can be sufficiently protected. Searchable FDA decisions online will make it easier for companies to obtain information about their competitors, potentially leading to infringement of intellectual property rights.

"Developing a web-based Network"

BIOCOM has strong concerns related to CDRH's recommendation to utilize outside experts using social media technology to assist staff in understanding technologies. CDRH should enhance its support for training and professional development for review staff, but utilizing outside experts through social media could lead to confidentiality issues, conflict of interest, FACA issues and subject manufacturers to accusations related to marketing inappropriately or promotion of off-label uses. More information is needed and BIOCOM believes any experts leveraged to assist FDA staff should be from a broad range of industry, academia and VC backgrounds, and should be fully transparent in their roles.

BIOCOM respectfully requests your careful consideration of our concerns listed above. Many of the proposed recommendations would force the industry to over-report, risk legal breach and may lead a costly and unnecessary burden on FDA and industry resources. BIOCOM appreciates the work effort the FDA, the Center, and the working group have expended to generate this report. We are confident the Agency will continue working with all stakeholders in an open manner. Thank you for your consideration.

Sincerely,



Joe Panetta
President & CEO
BIOCOM

BIOCOM

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SPS Medical Supply Corporation (Jennifer Griffin) – Comment (posted 11/02/10)

FDA-2010-N-0348-0070

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September 30, 2010

Division of Dockets
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Dear Food & Drug Administration,

Let me begin by thanking the Food & Drug Administration for this opportunity to help foster a more rigid and transparent Center for Devices and Radiological Health with the help of industry and the formed committees.

I along with key personnel within SPSmedical Supply Corp reviewed Docket Number **FDA-2010-N-0348** and have prepared the following statements in response to the committee's findings and recommendations. The below comments were generated from Volume 1of the 510(k) Working Group Preliminary Report and Recommendations published August 2010.

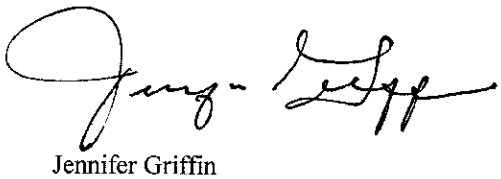
1. Page 5¶4: Development of a "class IIb" guidance – SPSmedical is in favor of developing a class IIb device classification for administration distinction purposes. Class II covers a wide range of devices, some far more textured than others. Making this distinction will help the reviewer in terms of required evidence to demonstrate substantial equivalence.
2. Page 6¶2: Enhancing internal and public 510(k) databases "with up to date" device information – SPSmedical opposes this recommendation due to several considerations. "Up to date" indicates that if a manufacturer makes a design change to a device that does not require a 510(k), this updated information however minimal will have to be updated in the 510(k) database Depending on the change the database may not have to be updated, but who makes that determination and how? Our concern is the FDA will be focusing on keeping databases up to date with information that is not necessarily required, when the energy can be better served on another front.
3. Page 8 •*Concerns about Predicate Quality*: Device no longer available for use as a predicate. – SPSmedical is neither for nor against, just a comment. If a device is deemed no longer able to be used as a predicate due to S&E concerns, does the manufacturer have to stop marketing the device? If the FDA allows the manufacturer to continue to market the device what kind of justification will the FDA have for doing so? And finally does the manufacturer have to re-file for S&E concerns?
4. Page 10 •*Unreported Device Modifications*: Clearer definitions – SPSmedical agrees with the committee's recommendation to revise for clarity the guidance document to clarify what types of modifications do or do not warrant a new 510(k). Currently the document is open to bias among manufacturers and decisions may not be made at the regulatory level. Additionally, SPSmedical agrees with defining exactly what modifications are eligible for a special 510(k). SPSmedical has recently filed for two traditional 510(k)'s when we feel only a special was required. There was no modification to the device itself only a labeling change to include a new sterilizer manufacturer(s) for a line of our chemical indicator products.

FDA-2010-N-0348

5. Page 13 – Limited Tools for Review Staff and Outside Parties – SPSmedical does not see the benefit of building a robust online public database. The term public infers that users will be referencing this database which is not at all a bad thing, but it is up to each manufacturer with original FDA approval to supply users with the most up to date information about their products. This information gets verified by consistent regular inspections at the manufacturer site. This would also burden manufacturers who private label product or have products private labeled for them.
6. Page 69 Section 5.2.1.1 Unreported Device Modifications – SPSmedical agrees with the issue of clarifying the guidance on when to file or not file for device modifications. We are strongly against the need for the manufacturer to provide regular, periodic updates to the Center for modifications which do not require a new 510(k). Better inspector training, more emphasis on regular site inspections and a clearer guidance within the manufacturer change document would far better serve the FDA and public health. This requirement would be over burdensome to the manufacturer and would provide little benefit to patient safety.
7. Page 72¶3: Not all CDRH review staff and submitters have an accurate understanding of how to properly use standards in 510(k) submissions. – SPSmedical firmly agrees with this statement.
8. Page 86¶4: The annual registration process is burdensome in and of itself. SPSmedical cautions the CDRH in maintaining a database of updated device labeling. Better inspector training, more emphasis on regular site inspections and a clearer guidance within the manufacturer change document would far better serve the FDA and public health. The lion's share of device labeling changes are minor in nature and this would add much unwarranted burden to the device manufacturer.
9. Page 87 Section 5.3.1 Expertise of reviewers: Reviews must be performed by a qualified reviewer or team of reviewers depending on the device. The submitter should be notified upon submission of the 510(k) who will be reviewing his/her submission. The individual or team of individuals reviewing the submission qualifications should also be public knowledge. This will open the door for a more transparent review process.

In closing, SPSmedical has a solid understanding of the standards, and guidance documents required to bring a product to market and the regulatory responsibilities required to market class II medical devices in the US. SPSmedical does not feel the FDA is using all of the resources currently available to them. Device manufacturers have a wealth of knowledge that can be used to educate FDA reviewers. The FDA should not be afraid to place a call to a device manufacturer who may be able to assist them with answering an unknown question. The FDA should revise current guidance documents which are what manufacturers directly use to design and develop medical devices. This teamed with rigorous training for reviewers and inspectors along with performing regular site inspections will ensure safe and effective products.

Sincerely,



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LifeScience Alley (LSA) (Donald Gerhardt) – Comment (posted 11/02/10)

FDA-2010-N-0348-0071

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October 4, 2010

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http://www.regulations.gov

RE: LifeScience Alley comments regarding the Center for Devices and Radiological Health '510(k) Working Group Preliminary Report and Recommendations', and 'Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations'

Docket No. FDA-2010-N-0348

LifeScience Alley is Minnesota's association for the medical technology industry. Representing 640 companies and 250,000 Minnesotans, LifeScience Alley is the largest state medical technology association in the country. LifeScience Alley (LSA) acts as the industry's central resource for fostering innovation, offering education & networking, creating consensus, and providing a strong, unified legislative voice. Through our combined efforts we seek to advance medical technology for the benefit of patients everywhere.

LSA recognizes the key role played by CDRH in protecting public health and advancing innovation. The study by CDRH of the 510(k) system provides valuable information and insights into the strengths and weaknesses of the 510(k) process. CDRH is to be commended for the open and detailed assessment of the 510(k) process. LSA supports many of the concepts and themes set forth by CDRH including the importance of training, the need to improve the de novo process, and notification of transfers of 510(k) ownership. LSA endeavors to be a value added partner in all efforts to improve the 510(k) system. LSA appreciates the opportunity to comment on the proposed changes to the 510(k) system.

The '510(k) Working Group Preliminary Report and Recommendations' and the 'Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations' contain preliminary discussion topics and not specific proposals. LSA appreciates the opportunity to participate in providing comment and feedback, yet LSA fails to see how detailed comments on the general list of discussion topics presented by FDA can lead to a genuine and productive public comment on the issues. Below, LSA has chosen to comment on some of the more substantive issues due to their serious potential implications to policy and process. After FDA has actual proposals for each of these topics, LSA looks forward to an interactive and cooperative process through which the 510(k) process will be discussed and possible improvements vetted

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1. **LifeScience Alley is not aware of any evidence of a public safety concern that would generate a need for hasty or significant revision of the current 510(k) process.**

A recent University of Minnesota study presented at the Institute of Medicine (IOM) meeting this past summer demonstrated that the history of medical device recalls shows no emerging problem with the device review process.[1] To date, FDA has not indicated a need for any 510(k) rescission; even in the highly controversial case of the ReGen 510(k), a panel review supported the issuance of the 510(k). Evidence shows that the process works to provide patients with safe and effective medical devices. A key FDA guidance, "*Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1)*" issued in January 1997, has been helpful and frequently consulted by manufacturers for over ten years, resulting in cleared 510(k) submissions for tens of thousands of products with a solid history of safety and effectiveness. While specific examples within this guidance document may benefit from an update, the history of safety of Class II devices over the past decade shows that the basic concepts and algorithm in this and other 510(k) guidance documents and in 510(k) regulations work well and do not need major overhaul.

LSA has serious concerns about the manner in which 510(k) process improvements are being conducted and the possible ways in which the suggested changes might be implemented. FDA's request for comments on preliminary recommendations is unlike any of the regulatory changes that have taken place in the past decades. This is not an opportunity to comment on proposed regulation wording, or an opportunity to comment on the policy behind proposed guidance. We have been asked to comment on merely a list of concepts that FDA is considering, with no specific language or policy. These are not specific proposals, but rather topics for possible future action. Some topics, such as improved training for FDA staff, are not controversial and would likely generate broad public support. Other topics, however, could signal major changes in the manner in which medical devices reach the patient. In order for public comment to be a meaningful process, each substantive item should be subject to separate public comment after FDA has established specific proposed language or policy regarding the issue. Without a discussion of these specifics, the comment process is of little value.

LSA is also concerned that some of the recommendations are already being implemented within CDRH without public discussion, or even public notice. Changes in the acceptance of predicates, for example, have been made with no public announcement. We are concerned that the list of recommendations will lead to further silent adoption of new or changed policy within the Center.

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[1] Study results presented at IOM Meeting 3 Public Health Effectiveness of the FDA 510(k) Clearance Process, July 28, 2010, see http //www.iom.edu/~/media/Files/Activity Files/PublicHealth/510kProcess/2010-JUL 28/06 Hall.pdf

Each of the suggested changes could result in a positive impact that could help patients by fulfilling FDA's statutory mandate to take "appropriate action on the marketing of regulatory products in a timely fashion." On the other hand, each could be used in a manner to further slow down the 510(k) process and prevent US patient access to modern medical treatments. Each topic of discussion has the opportunity to add clarity and certainty to the process, but each also has the risk of adding layers of unneeded bureaucracy and delay.

Recommendation

LSA requests that these major changes in the 510(k) program be discussed and evaluated in an open public forum and not as part of internal FDA policy. Some should take the form of regulation, such as changes in the definition of intended use and indications for use. Some should be embodied in guidance, with an opportunity for public comment. None of the substantive changes should be undertaken within FDA out of the public eye and without public input.

LifeScience Alley (LSA) supports continued refinement of regulatory processes, in general, and supports modifications to the 510(k) process that improve efficiency. FDA's internal policies and practices are slowing down the 510(k) process. Through unneeded excess data demands FDA is creating a more burdensome process. FDA has created a new era of uncertainty, where no device company can predict how to get needed innovative medical devices to patients.

2. **LSA supports clarification of *Indications for Use* and *Intended Use* and requests that FDA use notice-and-comment rule making processes if proposing definitional changes in regulation to clarify these terms.**

LSA supports clarification of the definitions of *Indications for Use* and *Intended Use* and opposes combining the terms into one. Currently there are various existing regulatory definitions that would require formal notice-and-comment rulemaking to make any changes.

Intended Use and *Indications for Use* are defined as requirements for inclusion in market authorization submissions. Specifically, *Intended Use* is defined in the 510(k) regulation while *Indications for Use* is defined in the PMA regulation. While the definitions have some similarities, by policy and practice these terms have evolved different meanings and interpretations. FDA now requires that both be used in the 510(k) process.

Compare *Intended Use* in 21 CFR 807.92 for requirements for contents of a 510(k):

> A statement of the intended use of the device that is the subject of the premarket notification submission, including a general description of the diseases or conditions that the device will diagnose, treat, prevent, cure, or mitigate, including a description, where appropriate, of the patient population for which the device is intended.

...with *Indications for Use* in 21 CFR 814.20 for requirements for contents of a PMA:

> A general description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended.

Intended Use is defined by many FDA and regulatory experts as being more general than *Indications for Use*, and *Indications for Use* is thought of as more disease-specific. However, FDA requirements have appeared to require, without change to regulation or guidance, increasingly more specificity in both *Intended Use* and *Indication for Use*. No matter what definition is used, the term "general" appears to no longer be in effect. While the regulation requires that a 510(k) application include a statement of *Intended Use,* FDA also expects *Indications for Use* to be included in the 510(k) application and labeling. Then FDA issues a Substantial Equivalence letter for the 510(k), with an addendum attached, specifying *Indications for Use*.

Thus these two terms have evolved into the 510(k) process through practice and not by law. LSA believes that current concepts benefit public health and provide important policy distinctions but they should be more explicitly defined.

Recommendation

LSA recommends that FDA revisit the term "general" in the definitions and change its practice to follow the existing regulation. If this is achieved, LSA urges that FDA use the Good Guidance Policy to frame definitions upon which industry and FDA can agree. Since the current practices have no foundation in the regulations as they stand, LSA suggests that FDA use notice-and-comment rule making processes to update the regulations to conform to FDA practice.

3. **LSA supports clarification of the terms 'different technological characteristics' and 'different questions of safety and effectiveness', especially to clarify that whether a device raises 'different questions of safety and effectiveness' should be based on consideration of submitted data and other information.**

LSA recognizes the terminology inconsistencies between the statutory terms "different technological characteristics" and "different questions of safety and effectiveness," and the 510(k) guidance terms "new characteristics" and "new types of safety or effectiveness questions" and "new questions of safety and effectiveness." We agree that these inconsistencies could make it challenging to interpret the statutory review standard to determine when "different technological characteristics" raise "different questions of safety and effectiveness" when comparing the "technological characteristics" of a new device to those of a predicate. Terminology in FDA guidance could be clarified to use the same exact terms as the regulation

Industry and FDA reviewers generally have a practical and consistent understanding of what constitutes a 'different technological characteristic'. Table 5.2 in the 510(k) Working Group Preliminary Report and

Recommendations shows that, in response to the question *"Which of the following represent a change in the technological characteristics from the predicate device to the subject device? (Select all that apply.)"*, ODE reviewers and managers selected the same items most of the time. The inconsistent terms have not resulted in poor 510(k) clearance decisions by the majority of FDA reviewers or poor 510(k) submissions by the majority of medical device companies. Industry and FDA reviewers have followed the guidance since 1997 and most cleared Class II medical devices have not been associated with a history of serious injury or failure to achieve their intended clinical use.

FDA 510(k) guidance is in agreement with 21 CFR 807; both require that the 510(k) submission —

- Establish that the subject and predicate devices have substantively the same intended use
- Compare technological features
- Provide data from testing and other analyses to demonstrate that the technological differences do not raise different questions of safety and effectiveness.

Recommendation

LSA believes there is a need to clarify that the determination of whether a device raises a different question of safety and effectiveness should be made after taking into account submitted data from testing and other analyses that address the technological differences. The following simple example illustrates this for the device in the case study, a powered dental hand piece:

- Both the air-powered and electrically powered devices are intended to cut, smooth, and polish tooth structure
- A feature comparison would reveal a technological difference in the means of powering the device.
- Electrical safety testing would be performed following standardized methods. The test results would be judged using industry standard acceptance criteria. The results would be considered in a risk assessment following industry standard risk management techniques. The conclusion would be that the risk of patient injury posed by the electric power source is acceptably low and not greater than the risk posed by the air power source.
- The electrically powered device would, therefore, have been shown to raise no different questions of safety and effectiveness, after taking into account the submitted test data and risk assessment summary.

A device that raises new questions of safety and effectiveness is one for which a rigorous, industry-standard risk assessment fails to result in a risk profile that is at least as low as the predicate device type. For example, a dental hand piece powered by a source for which there was no industry standard acceptance criteria or test method may raise new questions of safety or effectiveness (and therefore be a candidate for the de novo process).

4. LSA supports streamlining the de novo process and establishing a generic set of controls.

The possibility of streamlining and establishing a special set of product specific controls for devices classified into Class II through the de novo process may be beneficial to both industry and FDA. The legislative history of this provision contemplates a process that permits the FDA to reclassify certain low risk devices into Class I or II on the basis of established risk-based classification criteria when a new device is classified into Class III under the statute because there is no predicate device to which it can be found substantially equivalent. Congress included this section to limit unnecessary expenditure of CDRH and manufacturer resources that could occur if low risk devices were subject to premarket approval (PMA) under section 515. The section was not intended to significantly increase the number of NSE (not substantially equivalent) determinations or to otherwise alter the 510(k) provisions of the Act or CDRH's approach to the 510(k) classification process.[2]

Recommendation

LSA recommends streamlining the de novo process and establishing a special set of controls for devices undergoing the de novo process if the outcome includes the following:

- Use of the existing 513(g) process to establish a de novo classification and the type of supporting evidence needed to gain 510(k) clearance
- Guidance on —
    - Information to be included in a de novo 510(k) that the FDA will accept as evidence that the reasonable assurance of safety and effectiveness standard is met, and
    - How risk-based special controls can be implemented through performance standards, post-market surveillance, and/or patient registries, including guidelines for the submission of clinical data, possibly including OUS clinical data in premarket notification submissions in accordance with section 510(k)
- Elimination of the NSE review cycle allowing the de novo process to proceed more efficiently
- Allowing for product specific guidance, if needed, to be developed after completion of the initial de novo review process for a product type

5. LSA generally supports better FDA understanding of a 510(k) device under review, but does not agree that any device should be available to FDA during future reviews.

LSA supports FDA access to a 510(k) device that is under review. However, as with all topics in the 510(k) Working Group Preliminary Report and Recommendations, the recommendation is broad and does not

[2] New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff Section 207 (FDAMA); Section 513 (f)(2) of the FDCA; 21 USC 360c(f)(2)

specify how FDA might access devices under review. LSA recommends that this requirement be more thoroughly specified and open to public comment before implementation.

Many devices are sufficiently small, (a catheter, for example) enabling a single device to be shipped to FDA during the review process for reference. However, shipping a large device, such as a computer imaging system console, to FDA would be impractical and expensive and FDA would not likely have appropriate accommodation. Units shipped to FDA would require secure area to store the devices, and electromedical equipment would require utilities. Considering that thousands of devices are reviewed by FDA annually, this would become a significant storage burden and cost for the agency. Likewise, it is simply not feasible for companies to be required to maintain physical specimens for some indefinite time period.

Instead, LSA recommends that FDA continue to implement and broaden their site visit program, whereby, for complex devices, the FDA review team visits the manufacturing site to see the device, how it is made, and how it works. In addition to site visits, FDA should continue to host "vendor days," providing the opportunity for manufacturers to bring their devices to FDA. Most manufacturers would prefer to demonstrate their device to the FDA review team to provide clarity and understanding to the product review process that may not be obtainable from pictures and diagrams of the device. For less complex products LSA believes an opportunity to present and discuss a device and its use with the FDA reviewer(s) using web meeting tools would greatly benefit the review. Manufacturers appreciate the challenges associated with not physically seeing and handling the device, and the benefit of having the reviewers get the "touch and feel" of the product. Questions are often received that could be resolved through a device demonstration. This approach could be administered by the FDA reviewer contacting the manufacturer within 30 days of the 510(k) submission and requesting a device demonstration, or by the submitter requesting an opportunity to demonstrate the device in the submission cover letter.

After a device is cleared for use, it should not be allowed to be examined in support of future reviews on behalf of other companies, regardless of whether it is cited as a predicate device. FDA would need to properly store these devices so that access would be available whenever another manufacturer cites the device as a predicate. This is impractical for the reasons mentioned above. Excessive handling of the device by FDA reviewers could damage the device by subjecting it to forces and movements for which the device was not designed. Although the recommendation suggests that manufacturers provide one device for FDA access, if the device is to be available during each review where it is cited as a predicate, it is inevitable that FDA would request or require additional units. Depending on the device, this could lead to an unnecessary expense for the manufacturer. A manufacturer should not be held responsible for the expense associated with the review of a competitor product.

Recommendation

In general, LSA supports FDA access to a 510(k) device that is under review. However, as with all topics in the 510(k) Working Group Preliminary Report and Recommendations, the recommendation is broad

and does not specify how FDA might access devices under review. LSA recommends that this requirement be more thoroughly specified before implementation. LSA does not support any requirement to maintain a physical specimen after clearance.

6. **LSA believes that Special Controls Guidance can continue to be used effectively, dynamically, and flexibly to communicate FDA's market authorization requirements for 510(k) devices, and that a new classification such as 'IIb' is unnecessary, overly complex and rigid.**

LSA recognizes the range of product complexity and risk profiles in the Class II category. LSA believes that FDA has successfully used Special Controls, such as guidance, to communicate its market authorization expectations for the variety of products in Class II with their inherent wide-ranging complexities and risk profiles. The use of guidance can continue to be used effectively, dynamically, and flexibly for this purpose. Establishing a new product category "IIb" would require the FDA to make rules regarding which devices fall into this sub-class; rules that may be outdated before long because neither the FDA nor industry can foresee new technologies currently undefined. General guidance for the totality of devices in a new class IIb category will likely be insufficient to result in submissions that satisfy the FDA; product-specific guidance will still be needed. LSA believes a new Class IIb category adds complexity with no value to the 510(k) review process.

Recommendation

LSA recommends that FDA develop guidance as an effective means to communicate current FDA expectations to industry; this allows the FDA more flexibility to keep up with innovative technologies. When needed, the guidance should specify the types of clinical data that could meet the definition of valid scientific evidence and would therefore be sufficient to demonstrate substantial equivalence. The need for clinical data should be based solely on whether there is field data indicating a safety concern for that technology or device type (e.g., infusion pumps). Various types of clinical evidence should be allowed, including: clinical data from published literature, single arm registry studies, treatment-only studies using published predicate data as a historical control, concurrent control trials, and proprietary clinical data that adequately addresses safety objectives.

7. **LSA believes the FDA lacks legal authority to dictate IDE study designs to sponsors and investigators as long as the design is safe and scientifically credible, but LSA is in favor of improving the efficiency of IDE reviews.**

LSA is concerned about the recommendation to *"continue efforts to improve the quality of the design....of clinical trials to support PMA's"* because no specific improvement efforts have been announced or communicated to industry using legally-defined communication mechanisms and accompanying public comment periods. In accordance with 21 CFR 812.30(b)(4), FDA lacks authority to disapprove IDE applications unless (i) the risks outweigh the benefits to the patient (i.e., patient safety), or (ii) the trial design is scientifically unsound. These criteria have been in place and utilized by trial

sponsors (both academic and industry) since shortly after the 1976 Medical Device Amendments to the Food, Drug, and Cosmetic Act. However, CDRH is apparently not currently approving IDE applications if the reviewers have concerns as to whether the trial will result in a PMA approval. This mandate appears to have resulted in virtually no new IDE applications being approved by ODE. This unilateral directive informally established a major additional criterion that has no regulatory basis. Further, this position is scientifically flawed in that it presumes that ODE personnel have the unique prescience to determine the outcomes of clinical research prior to the studies actually being executed and the data evaluated by the FDA and the medical community.

Recommendation

LSA recommends that FDA make public the legal analysis that supports its position on the criteria for approving IDE applications. If legal authority is not present, FDA should expediently approve IDE applications that are being delayed solely on the basis of the Director's informal directive. LSA also recommends that FDA feedback on study designs have a clear scientific basis, grounded in publically available, peer-reviewed scientific literature.

LSA applauds the FDA recommendations to analyze methods for improving the efficiency and effectiveness of the pre-IDE process and the IDE review process. LSA additionally lauds FDA for recommending an analysis of methods for meeting the statutory requirement of a complete review within 30 days. Current FDA practice seems to be a partial review of IDE applications, followed by a disapproval letter to the sponsor stating that the sponsor must acknowledge that FDA may find additional deficiencies as it continues its review of the IDE application. Perhaps the FDA has at times misdirected its IDE review resources trying to re-design trials for sponsors rather than focusing on the safety and scientific credibility of sponsors' study designs. LSA recommends that FDA follow current regulatory requirements in its review of IDE applications.

8. **LSA supports the continued use of multiple cleared devices in 510(k) submissions to establish substantial equivalence for technological advances in Class II devices.**

FDA has already begun an informal process of restricting multiple predicates in the determination of substantial equivalence. Thus, the reference to it in the FDA recommendations is not a new proposal, but a proposed formalization of practices already in place. LSA opposes a restriction on the use of multiple cleared devices, both in current practice and in future policies.

While there may be occasional cases of an unduly large number of predicates, LSA believes the use of multiple cleared devices is necessary to implement the statutory definition of substantial equivalence. In Section 513(i) the Food, Drug, and Cosmetic Act, the test for substantial equivalence has two elements: first, whether the device has the same intended use as the predicate and second, whether new technology is as safe and effective as the predicate and does not present new questions of safety and effectiveness. This second element may require additional evidence and the most common way to provide this has been to show safe and effective use of the technology in another legally marketed

device. The definition supports one of the most important development practices in Class II products: use of a technology proven on one type of device to improve a device with a different technology. To ban this practice would require new, useless, duplicative research to reprove concepts which are already known and have been cleared by FDA.

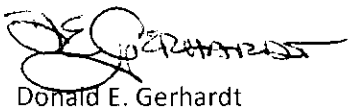
Recommendation

LSA urges caution in *unnecessarily* restricting the use of multiple cleared devices (to 5 or any other number) in that it will seriously threaten incremental technological advancements in Class II devices. Eliminating the use of multiple cleared devices would essentially rewrite the second element of Section 513(i), which cannot be done with guidance. FDA would be requiring essentially the same standard as for a PMA: original research.

Conclusion

LifeScience Alley supports continued refinement of regulatory processes, in general, and modifications to the 510(k) and IDE processes that improve efficiency. We look forward to an interactive and cooperative process by which industry and all other stakeholders will be notified of specific FDA proposals to change guidance or regulation and be given a reasonable opportunity to comment.

Sincerely,



Donald E. Gerhardt
President & CEO

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Boston Scientific Corporation (Sheila Hemeon-Heyer) – Comment (posted 11/02/10)

FDA-2010-N-0348-0072

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2010 OCT -5 A 9:35

October 4, 2010

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Submitted electronically and via FedEx

RE: Boston Scientific Corporation Comments to Docket No. FDA-2010-N-0348 CDRH Preliminary Evaluations, 510(k) Working Group Preliminary Report and Recommendations, and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations

Dear Sir/Madam:

Boston Scientific Corporation appreciates the opportunity to submit these comments in response to the Center for Devices and Radiological Health (CDRH) Preliminary Internal Evaluations, 510(k) Working Group's Preliminary Report and Recommendations, and the Task Force on the Utilization of Science in Regulatory Decision Making (the "CDRH recommendations") released August 4, 2010.

Boston Scientific is a worldwide developer, manufacturer and marketer of medical devices. For more than 30 years, Boston Scientific has advanced the practice of less-invasive medicine by providing a broad and deep portfolio of innovative products, technologies and services across a wide range of medical specialties. The Company's products help physicians and other medical professionals improve their patients' quality of life by providing safe and effective alternatives to surgery.

Boston Scientific commends FDA for taking a critical look at the 510(k) program and for identifying areas for improvement within CDRH. We recognize that many of the CDRH recommendations will benefit both industry and the Agency. The recommendations relating to enhancement of training for CDRH review staff, additional clarification for certain terms related to the 510(k) program, and streamlining the guidance and de novo 510(k) processes should improve the consistency and predictability of the 510(k) program. We offer our assistance, as

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appropriate, in developing new training programs and guidance documents and request that internal CDRH training programs on regulatory processes also be made available to industry. Consistent training for both CDRH and industry will promote mutual understanding and application of the regulatory requirements, ultimately benefiting patients by enabling timely approvals of safe and effective medical devices diagnostics, and combination products.

Boston Scientific is a member of both the Advanced Medical Technology Association (AdvaMed) and the Medical Device Manufacturers Association (MDMA), and we endorse the positions articulated in their comments submitted to the FDA docket in response to the CDRH recommendations. However, we would also like to take this opportunity to provide our own comments on specific areas of concern to Boston Scientific. We recognize that the CDRH recommendations are preliminary and lack the detail necessary for a full impact assessment. Boston Scientific looks forward to providing more detailed input once CDRH has reviewed all comments and determined which recommendations to move forward with more detailed proposals.

The 510(k) Working Group recommends that CDRH revise existing guidance to consolidate the concepts of "indications for use" and "intended use" into a single term, "intended use".

Boston Scientific supports the need to clarify the definitions of and provide additional guidance for the appropriate uses of the two terms, *intended use* and *indications for use*. However Boston Scientific does not support consolidating the two terms into the single term, *intended use*.

The terms *intended use* and *indications for use* have distinctly different meanings and are both integral to the 510(k) program. The FDA *Guidance on the CDRH Premarket Notification Review Program 6/30/96 (510(k) Memorandum #K86-3)* clearly delineates the differences between these terms. The guidance states, "While a new device must have the same intended use as a predicate device in order to be SE, the Center does not require that a new device be labeled with precise therapeutic or diagnostic statements identical to those that appear on predicate device labeling in order for the new device to have the same intended use. Label statements may vary. Certain elements of a predicate device's labeled indication may not be critical to its intended therapeutic, diagnostic, prosthetic surgical, etc., use . . .. Thus, a new device with the same intended use as a predicate device may have different specific indication statements, and, as long as these label indications do not introduce questions about safety or effectiveness different from those that were posed by the predicate device's intended use, the new device may be found SE."

Intended Use is a statement of what the device does or the claimed purpose of the device. As established by law, a new device evaluated under the 510(k) regulations must have the same intended use as the named predicate device(s) in order to be found substantially equivalent. By

comparison, *indications for use* may set forth specific information to further define, for example, different use environments, patient populations, disease states, or methods of use. A new device with different indications for use can still be found substantially equivalent to a predicate device as long as the intended uses are the same and the differences in indications for use do not introduce different questions of safety or effectiveness (see *K86-3*). By consolidating the two terms into one, this distinction would be lost with the result that any change to a device's indications for use, even if the change did not raise different questions of safety or effectiveness, would render that device not substantially equivalent (NSE). This situation would be the antithesis of one of the principles set forth for the 510(k) program in the K86-3 Memorandum, "If substantial equivalence were judged too narrowly, the marketing of devices that would benefit the public would be delayed; the device industry would be unnecessarily exposed to the greater burdens of premarket approval; new devices would not be properly classified; and new manufacturers of pre-Amendments type devices would not have marketing equity."

Boston Scientific concludes that the distinctions between a device's *intended use and indications for use* are important for successful application of the 510(k) program and its principles. The two terms should remain discrete, but with clear definitions, guidance, and training. We suggest that the liberal use of examples will be beneficial to clearly explaining the differences between these two terms as well as the threshold for when different indications for use raise different questions of safety or effectiveness and would render a device NSE.

The 510(k) Working Group recommends that CDRH explore the possibility of pursuing a statutory amendment to section 513(i)(1)(E) of the Federal Food, Drug and Cosmetic Act (21USC§360c(i)(1)(E)) that would provide the agency with express authority to consider an off-label use, in certain limited circumstances, when determining the "intended use" of a device under review through the 510(k) process. Such circumstances would include the availability of compelling evidence that the primary use of the marketed device will be off label.

With the enactment of FDAMA, Congress provided clear direction and limits on how the Agency may address potential off label use of devices undergoing 510(k) review. Congress was clear that CDRH could not withhold 510(k) clearance on the basis that the device might be used off-label. Instead, the Food Drug & Cosmetic Act (FDCA) was revised to give CDRH the authority to issue a "Substantial Equivalence with Limitation(s)" decision and require a warning statement in the device labeling if CDRH determines there is a reasonable likelihood that the device will be used off-label and that the off-label use could cause harm. Thus, Congress upheld two longstanding principles that: 1) the FDCA cannot be used to regulate off-label use by a healthcare practitioner ("[n]othing in this Act shall be construed to limit or interfere with the authority of a healthcare practitioner to prescribe or administer any legally marketed device to a

patient for any condition or disease within a legitimate healthcare practitioner-patient relationship" (see FDCA § 906)); and 2) that a device's intended use is determined by the "objective intent of the persons legally responsible for the labeling of devices" (see 21 CFR 801.4). As long as the intended use put forth in the 510(k) is bona fide for the device, 510(k) clearance should not be withheld because healthcare practitioners may use the device off-label. The current SE with Limitation(s) program strikes an appropriate balance as it does not interfere with the practice of medicine, but does convey important information about the status of a potential off-label use for the device or diagnostic.

Since 513(i)(1)(E) was implemented via FDA guidance in 1998, a total of 306 SE With Limitation(s) decisions have been issued through July of 2010 (see CDRH Releasable 510(k) Database at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm). This total includes limitations related to potential off-label use as well as for other reasons, such as warnings related to potential adverse events. In the same time period, nearly 48,000 510(k)s were found to be substantially equivalent and cleared for marketing. Therefore, the SE with Limitation(s) decisions represent less than 0.6% of the total SE decisions. These data indicate that concerns with potential off-label use arise in a very small percentage of 510(k) decisions and call into question the need to change the current Congressional framework and FDA practices for handling potential off-label use of 510(k) cleared devices and diagnostics.

The 510(k) Working Group recommends that CDRH consider developing guidance on when a device should no longer be available for use as a predicate because of safety and/or effectiveness concerns. It is expected that such a finding would be an uncommon occurrence.

Boston Scientific welcomes CDRH guidance documents that assist CDRH reviewers and industry to better understand and comply with applicable FDA regulations. However, such guidance must be in support of current law and regulation, and not be in lieu of formal process for creating new regulatory requirements.

With respect to the issue of appropriate predicate devices, Section 513(i)(2) of the Federal Food Drug and Cosmetic Act already establishes that, "A device may not be found to be substantially equivalent to a predicate device that has been removed from the market at the initiative of the Secretary or that has been determined to be misbranded or adulterated by a judicial order" (see also 21 CFR 801.100)(b)(3)). The law ties the criteria for when a device can no longer be used as a predicate to situations in which the device has been removed from the market via established administrative or judicial process. While additional guidance on this process may be helpful, Boston Scientific is concerned that the recommendation as stated implies an attempt to broaden the law by lowering the threshold currently established in 513(i)(2).

Removal of a legally marketed device as a lawful predicate is a serious issue and one with significant downstream consequences, raising questions about the marketing status of devices that had previously used the removed device as a predicate but may not have the same safety or effectiveness concerns. Boston Scientific urges CDRH to restrict such actions to circumstances contemplated by the current law and, even then, only when necessary to protect the public health.

The 510(k) Working Group recommends that CDRH consider issuing a regulation to define the scope, grounds, and appropriate procedures, including notice and an opportunity for a hearing for the exercise of its authority to fully or partially rescind a 510(k) clearance. As part of this process, the Center should also consider whether additional authority is needed.

As stated in the CDRH recommendations, the Agency already has "inherent authority to reconsider their decisions in certain circumstances, such as where there has been fraud or error, and to rectify their mistakes." Boston Scientific supports a regulation that would provide clear criteria and process, including notice and an opportunity for hearing, for CDRH to exercise this inherent authority with respect to 510(k) decisions. However, Boston Scientific believes that full or partial rescission of a 510(k) clearance should only be available as an Agency remedy if it is determined that a 510(k) Notification had included fraudulent information relied on for the SE decision or omitted material information that, had it been included in the submission, would have resulted in an NSE decision. Absent fraud or omission, 510(k) rescission should not be used as a way to subsequently address device safety or efficacy concerns. If safety or efficacy concerns rise to the level of serious risk to public health FDA should use its recall authority under 21 CFR 810, or other available enforcement tools such as injunction or seizure, to remove unsafe devices from the market.

As an accompaniment to any new regulation, FDA should provide detailed guidance as to how a rescinded 510(k) clearance, due to fraud or omission, will affect legally marketed devices that used the device subject to the rescission as a predicate. A 510(k) rescission could set off a cascade of events that could call into question the clearance of every product that identified the rescinded device as a predicate, as well as all subsequent devices that used those products as predicates, creating the potential for safe, beneficial devices to be removed from the market.

The 510(k) Working Group recommends that CDRH develop guidance on the appropriate use of more than one predicate, explaining when "multiple predicates" may be used. The Center should also explore the possibility of explicitly disallowing the use of "split predicates".

Boston Scientific supports the proposal that FDA develop guidance on the appropriate use of multiple predicates. However, Boston Scientific does not agree that FDA should explicitly disallow all use of "split predicates". Split predicates, or the use of one predicate for the

intended use and another for new technological characteristics, may be appropriate in certain circumstances.

Per the 510(k) regulations, a device with the same intended use can be found substantially equivalent to a device with different technological characteristics as long as the information submitted in the 510(k) demonstrates that the different technological characteristics do not raise different questions of safety or effectiveness and the new device is at least as safe and effective as the predicate device. The need for split predicates may arise when a new device has the same intended use as a legally marketed predicate, but different technological characteristics. A second device, previously cleared by 510(k) may be useful to show that the technical characteristics of the new device do not raise different questions of safety or effectiveness, even if the second device has a different intended use. A hypothetical example could be the case in which a new device has the same intended use as a legally marketed predicate but is made of a different material. A second device made of the same material as the new device and used in the same location in the body but for a different intended use, may be appropriate to answer questions about the new material. A 510(k) that uses split predicates must still satisfy the substantial equivalence criteria. If FDA believes that the information and test results presented in the 510(k) do not support a substantial equivalence determination and the device is in fact novel, FDA has the authority to find the new device NSE, and the sponsor has the option of the de novo classification process. Boston Scientific recommends that split predicates remain an option for industry, but that the Agency develop clear guidance to define the terms "multiple predicates" and "split predicates," the differences between the two, and the circumstances under which their use is acceptable.

The 510(k) Working Group recommends that CDRH explore the feasibility of requiring each manufacturer to provide regular, periodic updates to the Center listing any modifications make to its device without the submission of a new 510(k) , and clearly explaining why each modification noted did not warrant a new 510(k).

Boston Scientific does not support the proposal as stated. Additional clarity is needed to identify the types of modifications considered for the scope of this recommendation and the benefit the information would provide.

The FDA guidance document, "*Deciding When to Submit a 510(k) for a Change to an Existing Device (K97-1)*" has been in existence since January 1997, providing clear guidance as to the types of changes that can be made to a 510(k) cleared device without needing to file a new 510(k). The policies and procedures in this guidance were adopted by FDA because the Agency understood that many changes are made to devices for a variety of reasons that do not significantly affect the safety or effectiveness of the device and do not warrant FDA review or pre-approval. Manufacturers are required to have procedures in place to assess each individual

change for 510(k) submission requirements and internally document the rationale for each change that is determined to not require a new 510(k) in accordance with the FDA criteria. In addition, each change must be assessed collectively with all prior changes made since the 510(k) clearance to determine if the threshold for filing a new 510(k) has been triggered. FDA can audit a company's internal system and documentation of decisions made with respect to such changes to 510(k) cleared devices during quality system inspections.

It is not clear what additional benefit or protection to public health would be gained by requiring manufacturers to submit periodic reports to FDA documenting all changes not submitted in new 510(k)s. Given the thousands of devices and diagnostics that are currently on the market via the 510(k) process and the fact that such devices may undergo minor changes every year, the volume of data generated by this requirement would be significant and potentially overwhelming for current CDRH resources. While companies are already required to keep internal documentation of all changes and the associated rationale for those not submitted in a new 510(k), the work to compile all of this information into a coherent report each year would also be significant. Boston Scientific requests that CDRH consider this recommendation very carefully and not move forward with implementation unless and until the need for these periodic reports is clearly established, with evidence that such reporting is needed to protect public health, and sufficient CDRH resources are in place to review and make appropriate use of the information in the reports.

The 510(k) Working Group recommends that CDRH consider revising 21 CFR 807.87 to explicitly require 510(k) submitters to provide a list and brief description of all scientific information regarding the safety and/or effectiveness of a new device known to or that should be reasonably known to the submitter.

Boston Scientific does not support this recommendation as it is an overly broad requirement to meet the 510(k) standard of Substantial Equivalence.

Under current law and regulation, a 510(k) Premarket Notification must include all information that is material to the decision of Substantial Equivalence. Every 510(k) must include a signed Truthful and Accurate Certification by which the submitter certifies that all information in the 510(k) is truthful and accurate and that no material fact has been omitted. If the CDRH reviewer believes that there is insufficient information in a 510(k) to arrive at a decision, the reviewer has the option to issue a Request for Additional Information. If CDRH determines that a 510(k) includes false information or omits material information, then administrative and enforcement remedies are available. If CDRH has concerns that industry is not complying with the data requirements for 510(k), then perhaps better guidance, training, and communication will improve the quality of 510(k) submissions.

The CDRH recommendation as written would significantly broaden the current data standard for 510(k) to include "all scientific information regarding the safety and/or effectiveness of the device known to or that should be reasonably known to the submitter," and would require that this broad array of information be included in the initial submission, even if the information is not material to the Substantial Equivalence decision. This recommendation moves the data requirements for 510(k) into the realm of those required for PMA with the associated standard of "reasonable assurance of safety and effectiveness."

If CDRH has determined that certain types of information, necessary for an SE decision, are absent from the required contents of a 510(k) Premarket Notification, an alternative approach would be to update 21 CFR 807.87 to specify the additional necessary information. This should be done through the notice and comment process enabling stakeholders the opportunity to comment on the specific recommended changes.

The 510(k) Working Group recommends that CDRH develop guidance defining a subset of class II devices, called "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.

Boston Scientific supports the goal of CDRH to provide clarity and predictability as to the types of devices in Class II for which clinical information may be necessary to support a substantial equivalence decision along with the rationale behind this need for each device type. Transparency and predictability to data requirements is essential for industry to plan for premarket testing requirements, timelines, and financial support needed to bring products to market. However, Boston Scientific is very concerned that this CDRH recommendation has raised the potential for manufacturing information and postmarket evaluations to be routinely required for certain Class II devices regulated by 510(k). Manufacturing information may be requested by CDRH if it is necessary to reach a substantial equivalence decision, but the need for this type of information in a 510k) should be rare. In addition, CDRH currently has the authority to require a manufacturer to conduct postmarket surveillance of a Class II device under Section 522 of the FDCA, but postmarket evaluation is not typically required to support a substantial equivalence decision. If the risk profile for a device is so unknown as to require this type of information, then the device may be more appropriately evaluated under the PMA regulations.

The increased clarity and predictability at the heart of this recommendation can be achieved if CDRH makes public a list of device types for which clinical information has been routinely required along with the associated rationale. This information would put manufacturers on notice that there may be increased requirements for a particular device and why, and enable manufacturers to initiate discussions with CDRH early in the device development process.

Boston Scientific does not support the creation of a new subclass, Class IIb. Defining a new subclass implies that products in this subclass will be regulated differently. Creating a new subclass may also make it difficult to reduce the requirements on device types once sufficient information is known about the device type to no longer warrant enhanced data requirements in order to reach a substantial equivalence decision and protect the public health.

The 510(k) Working Group recommends that CDRH clarify when it is appropriate to use its authority to withhold clearance on the basis of a failure to comply with good manufacturing requirements in situations where there is a substantial likelihood that such failure will potentially present a serious risk to human health, and include a discussion of pre-clearance inspections as part of its "class IIb" guidance.

Boston Scientific does not support the above recommendations because, with the exception of design controls, compliance with FDA's good manufacturing procedures (GMP) is not a pre-clearance requirement for a finding of substantial equivalence. 510(k) is a classification process, and a finding of substantial equivalence is based on comparison of intended use and technological characteristics to a predicate device, not on whether the device is manufactured in compliance with GMPs. In many instances, the commercial manufacturing facility for the device may not be operational at the time of clearance and, therefore, a pre-clearance inspection would not be possible.

FDA has considerable authority to inspect medical device manufacturers and to withhold distribution, or mandate a recall per 21 CFR 810, of any devices found to be adulterated for failure to comply with good manufacturing requirements if such a failure presents a serious risk to human health. However, withholding 510(k) clearance is not an appropriate sanction in such cases for the reasons stated above.

The 510(k) Working Group recommends that CDRH revise existing regulations to clarify the statutory listing requirements for the submission of labeling. CDRH should also explore the feasibility of requiring manufacturers to electronically submit final device labeling to FDA by the time of clearance or with in a reasonable period of time after clearance, and also to provide regular, periodic updates to device labeling, potentially as part of annual registration and listing or through another structured electronic collection mechanism. If CDRH adopts this approach, updated labeling should be posted as promptly as feasible on the Center's public 510(k) database after such labeling has been screened by Center staff to check for consistency with the device clearance.

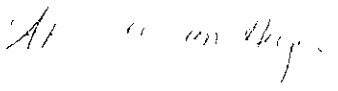
Current regulations require that each owner or operator required to register with FDA "maintain a historical file containing the labeling and advertisements in use on the date of initial listing" as well as "any labeling or advertisements in which a material change has been made any-time after initial listing" (see 21 CFR 807.31(a) and (b)). In addition, the owner or operator must be prepared to submit such labeling and advertising information to FDA upon request as specified in 21 CFR 807.31(e). Finally, FDA has authority to inspect all labeling and advertising materials to assure that they are being maintained in accordance with the listing requirements and that the information therein is in accordance with the intended use, indications for use, and claims as cleared by FDA.

Boston Scientific is unclear as to what additional benefit would be gained by requiring manufacturers to electronically submit all final device labeling, and periodic updates of device labeling, for 510(k) cleared devices. Given the thousands of 510(k) cleared devices on the market, this would create a significant amount of additional work for CDRH to review and process each labeling submission. Boston Scientific urges CDRH to consider this recommendation very carefully before implementing this broad requirement in light of the current authority already provided in 21 CFR 807.31 to request labeling and advertising as needed on a case-by-case basis.

Boston Scientific also does not understand the rationale for the CDRH recommendation to post all device labeling on its public 510(k) database. It is the manufacturer's responsibility to provide appropriate labeling to the appropriate end users and to assure that updated labeling is similarly distributed. Copies of labeling are available upon request or may be available electronically on a company website, targeted at the appropriate end users. The benefit for making all labeling publicly available for anyone to access on the CDRH database is unclear, especially for prescription devices when the labeling is intended for a licensed practitioner.

Boston Scientific would like to thank FDA for the opportunity to provide comments on the CDRH recommendations. We look forward to providing additional input as the implementation plans for the chosen recommendations are put forth for further notice and comment. We also offer our assistance to work together with FDA to assure robust, predictable processes that foster innovation, protect public health, and enable the delivery of safe and effective medical devices and diagnostics to patients around the world.

Respectfully Submitted,



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Best of Rowan, LLC (Steve Arey) – Comment (posted 11/03/10)

FDA-2010-N-0348-0073

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September 4, 2010

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[Docket No. FDA-2010-N-0348]

RE: Volume II "Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations."

- NEXT survey data has been performed since 1972 documenting average radiation doses using phantoms for common radiological exams including C.T. and pediatrics.
- MQSA was implemented in 1992 because of image quality concerns and enacted minimum phantom resolution standards.
- Image Quality was defined by the New Jersey State Division of Radiation Protection in 2005 with a state designed image resolution phantom.
- The wide spread use of CR and DDR prompted the MHRA to recommend manufacturers of digital equipment supply image receptor exposures which give the lowest possible patient dose for each particular examination and "prove these with an in-beam phantom during hand-over".
- Independent research: *"Comparing the Phantom Imaging Method with the Sensitometric Method as a Means of Testing Quality Control in the Film Processor"* Kendall C. Prescott, Catawba College, Salisbury, NC, Department of Chemistry, December 7, 2004; demonstrates a direct relationship between film screen and digital imaging. This research shows that a resolution phantom visual image adequately displays image details which are within the control ranges of sensitometry in medical x-ray film developing.

1. A Federal Standard Is needed that applies equally to film-screen and digital imaging with respect to image resolution and radiation dose. It must be simple to understand, require little additional training, and non-burdensome.
2. A phantom is manufactured from commercially available HDPE material having a specific gravity of .97. The amount of HDPE is the thickness that creates a radiographic image density equal to 23 cm. of water. Two halves make up an assembly having a combination of resolution details within the center. This phantom is equivalent to the NEXT survey test data for a 23cm average adult AP L/S spine exam.

FDA - 2010-N-0348 C

3. Additional resolution phantoms are available for the other NEXT common surveys which have been performed in the past.
4. In practice, each registrant owns a phantom equivalent to their modality.
    a. The phantom is imaged daily using the facilities equipment prior to exposing patients to ionizing radiation.
    b. An operator uses the technique which produces the best image their system is capable of.
    c. The image is processed and expected resolution objects are identified. The results are plotted graphically within a control window.
    d. Radiation dose for this exposure is compared to the NEXT survey data to ensure this equipment is below the national average radiation dose.

5. Any systems which cannot meet the minimum resolution and/or maximum radiation dose Standards, must be corrected or not allowed.
    a. Phantom imaging does not replace the need for annual calibration of the imaging system by a qualified and registered service company.
    b. Regulations should encompass both new and old equipment.
    c. Regulations should be simple to comply with and easy to understand.
    d. Testing should be done daily to insure systems maintain a minimum level of image quality and prevent unnecessary exposures.
    e. Image quality should be determined by reference to a National Standard not by individual imaging equipment manufacturers.
    f. Students of any discipline learn and retain knowledge most successfully if they see a meaningful relationship between the subject matter and their daily life.
    g. The application of a Standard methodology of this nature would enhance the scientific data of NEXT surveys.

Respectfully submitted,

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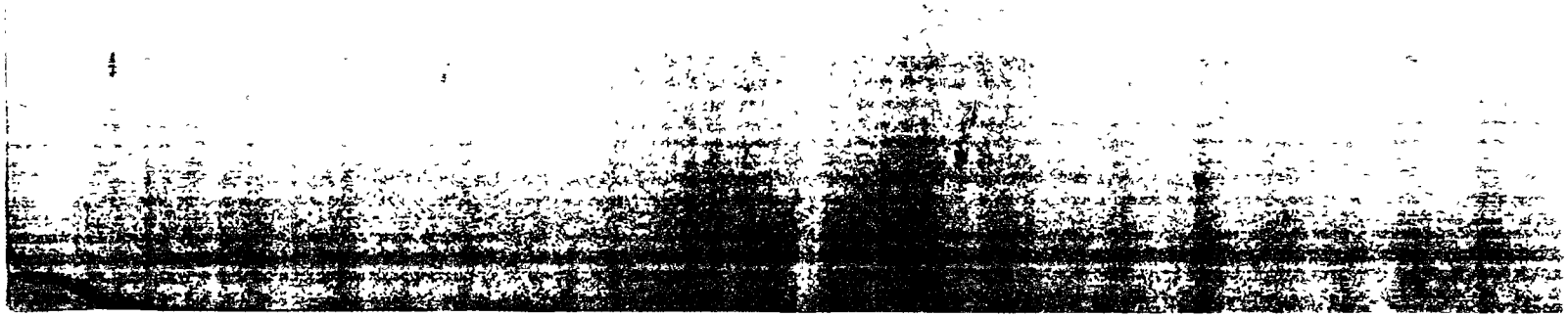
[Docket No. FDA-2010-N-0348]



The American College of Obstetricians and Gynecologists – Comment (posted 11/03/10)

FDA-2010-N-0348-0074

The American College of Obstetricians and Gynecologists (the College) applauds the U.S. Food and Drug Administration (FDA) and its Center for Devices and Radiological Health (CDRH) for considering improvements to the 510(k) process. The College is dedicated to the promotion of quality, safety, efficiency, and stability for the delivery of women's health care services. To that end, the College has an interest in supporting changes to the 510(k) process that will strengthen the FDA's ability to ensure the safety and effectiveness of medical devices.

Below are comments from College staff and members of the Committee on Gynecologic Practice on specific recommendations detailed in the August 2010 "Preliminary Report and Recommendations" issued by the 510(k) Working Group.

Volume I: 510(k) Working Group

5.1.2: The Working Group Recommendation: CDRH should explore the development of guidance and regulation to provide greater assurance that any comparison of a new device to a predicate is valid and well-reasoned.

- The College agrees with this recommendation.
- The College recommends that FDA consider restrictions when it allows an expansive view of same intended use in establishing predicate devices. For example, manufacturer A has developed a mesh for vaginal prolapse. Manufacturer B has a similar mesh on the market that is used in cardiac surgery. Manufacturer A should not be able to obtain clearance for its product unless it presents data from an IRB-approved trial in humans demonstrating patient safety when the product is used for vaginal prolapse. Clearance of the product should be contingent upon requiring a postmarket trial in which the product is compared to a "gold standard" to confirm efficacy.
- Clearance has been predicated on similar devices used in very different areas (the abdomen, a clean site, versus the vagina, a clean-contaminated site), which calls into question whether substantial equivalence has been met. Furthermore, general surgeons have a long history of declining to place mesh abdominally (for hernias) when vaginal surgery was being performed at the same time because of the concern regarding contamination, thus raising serious questions about whether or why a general surgeon would consider vaginal mesh to have substantial equivalence to abdominal mesh.

5.1.2.1 (Concerns about Predicate Quality):

- The College recommends that CDRH not permit citation as predicates devices withdrawn by their manufacturer for safety concerns.

- The College recommends that CDRH not permit citation as predicates devices no longer marketed unless compelling arguments exist.
- In addition, the 510(k) process should have a mechanism for managing significant reports of adverse effects in predicate devices, even if these predicates remain on the market. For example, once significant problems with similar vaginal meshes arose, it would seem that safety and efficacy of these predicates should have been demonstrated before further devices were cleared based on these predicates. The establishment of device registries to gather postmarket data on complications would improve the reporting of safety issues.

5.1.2.2 (Rescission Authority):

- The College agrees with the need for CDRH to issue regulations on its rescission authority. The fact that a proposed rule was issued in 2001, and yet a final rule was never issued, suggests both the need for additional staffing and oversight at CDRH.

5.2.1.2 (Quality of Submissions):

- The College agrees with the need for CDRH to require each 510(k) submitter to keep at least one unit of the device under review available for CDRH's use.
- The College agrees with the recommendation that CDRH require 510(k) submitters to include a list and brief description of all scientific information regarding safety or effectiveness of a new device known to or that should be reasonably known to the submitter.
- Regarding 21 CFR 807.87, which states that a 510(k) must include "[p]roposed labels, labeling and advertisements sufficient to describe the device, its intended use, and the directions for its use. Where applicable, photographs or engineering drawings should be supplied." The College supports the development of clearer guidance on the type and quality of training that is required to use devices. While adequate training guidelines exist for intrauterine devices and implants, such guidelines are lacking for vaginal mesh.

5.2.1.3 (Type and Level of Evidence Needed):

- The College agrees with the recommendation to implement a unique device identification (UDI) system.
- Once the UDI system has been established, the College strongly encourages the FDA to initiate a process to improve postmarketing surveillance that includes registering device use in an individual, so that clinicians and patients can report complications in a structure that has a numerator and a denominator. The collection of such data is essential to monitoring data for devices, especially for the case of vaginal mesh complications. There

is a need for section 522 studies as part of vaginal mesh follow-up. The FDA should consider mandating that industry fund surveillance of these devices via a registry.

5.3.1. (Continuous Quality Assurance: Working Group Recommendation: CDRH should enhance training, professional development, and knowledge-sharing among reviewers and managers, in order to support consistent, high-quality 510(k) reviews.

- The College supports this recommendation but also suggests that the most appropriate reviewers be assigned to each review. For example, the vaginal mesh submission should have been reviewed by the obstetrics and gynecology devices branch, not general and plastic surgery panel. Assigning less-complex reviews to ad hoc reviewer groups or third-party reviewers may be an effective means of optimizing CDRH staff resources.

5.3.1.1 (Reviewer Expertise and Experience):

- The College believes that the proposed Center Science Council can potentially increase consistency across CDRH and may improve quality of the reviews. However, the proposed Council also has the potential to add layers to reviews and extend the time from submission to clearance.

5.3.1.2 (Third-Party Review):

- The College recognizes the value of using third-party reviews (see comments on section 4.1.1.1, below) but advocates that third-party reviewers should be subject to the same conflict of interest process as staff reviewers.

Volume II: Task Force on the Utilization of Science in Regulatory Decision Making

4.1.1.1 (Premarket Review, least-burdensome provisions):

- The College agrees that the CDRH must have the authority to insist on having adequate information to fulfill its regulatory requirements.

4.1.1.1 (Premarket Review, review workload): Working Group Recommendation: The CDRH consider creating a standardized mechanism whereby review Offices could rapidly assemble an ad hoc team of experienced review staff from multiple divisions to temporarily assist with time-critical work in a particular product area, as needed, in order to accommodate unexpected surges in workload. This would need to be done in such a way

that ad hoc teams would only assist with work that does not require specialized subject matter expertise beyond what the team members possess. The Task Force recognizes that such an approach is only a stop-gap solution to current workload challenges, and that additional staff will be necessary to better accommodate high workloads in the long term.

- Although there are some benefits to the recommendation that a mechanism be established for creating ad hoc review teams from experienced review staff, this is—as noted in the proposal—a stop gap solution. Since the teams would be used for work that does not require specialized subject matter, a preferable alternative might be to make use of third-party reviewers for this work—assuming that they are appropriately trained and vetted for conflict of interest. Doing so would also avoid a trickle-down effect of delaying the experienced reviewers' other reviews.

4.1.3: Working Group Recommendation: CDRH should improve its mechanisms for leveraging external scientific expertise.

- The College would be very willing to work with the CDRH to help it obtain needed expertise. Our current collaborative relationship with the Ob-Gyn Devices Branch gives us an excellent foundation for such partnerships. The College's rigorous conflict of interest policy, which prohibits persons with conflicts of interest from serving on committees and in positions of leadership, will give the CDRH confidence in our ability to provide unbiased expertise. Such options should be given careful consideration and used whenever possible as a means of avoiding the otherwise inevitable conflicts of interest that attach to use of industry as a source of expertise.

4.3.1: Working Group Recommendation: CDRH should make use of more rapid communication tools to convey its current thinking and expectations.

Although the College recognizes the need for more rapid communication tools, it recommends against encouraging "industry and other constituencies" to submit proposed guidance documents. Because the guidance documents represent the FDA's current thinking on a topic, it appears inappropriate to outsource this effort to industry.

American Academy of Orthopaedic Surgeons, et al. (John Callaghan) – Comment (posted 11/09/10)

FDA-2010-N-0348-0075

AAOS
American Academy of Orthopaedic Surgeons
American Association of Orthopaedic Surgeons

November 4, 2010

Rec'd 11/8/2010

Margaret A. Hamburg, MD
FDA Commissioner
Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. FDA-2010-N-0348: Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations, and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability; Request for Comments

Dear Commissioner Hamburg:

The American Academy of Orthopaedic Surgeons (AAOS/Academy), on behalf of more than 17,000 Board-certified orthopaedic surgeons and with the support of the American Association of Hip and Knee Surgeons, the American Orthopaedic Foot and Ankle Society, the American Orthopaedic Society for Sports Medicine, the American Spinal Injury Association, the Arthroscopy Association of North America, the Cervical Spine Research Society, the Musculoskeletal Tumor Society, the Orthopaedic Rehabilitation Association, the Pediatric Orthopaedic Society of North America, the Ruth Jackson Orthopaedic Society, and the Scoliosis Research Society, commends the 510(k) Working Group and Task Force for their efforts, and thanks Director Shuren and FDA for soliciting stakeholder comment and town hall feedback. AAOS is dedicated to the development of sound federal health care policy that fosters patient access to the highest quality specialty care. As advocates for our patients, AAOS and specialty society members endeavor to provide the highest quality medical care.

Orthopaedic patients are daily benefactors of the success of the 510(k) program. As early as 1982, the National Institutes of Health (NIH) recognized total hip replacement surgery as "...a procedure which gives a predictably excellent result in the vast majority of patients" and noted that "Relief of pain and return to useful function can be expected."[1] The NIH's position was reaffirmed in 1994, when a second consensus conference found "Total hip replacement is an option for nearly all patients with diseases of the hip that cause chronic discomfort and significant functional impairment. Most patients have an excellent prognosis for long-term

[1] Total Hip Joint Replacement. NIH Consensus Statement Online 1982 Mar 1-3 [cited October 27, 2010];4(4):1-11.

Bone Joint Decade

FDA-2010-N-0348

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improvement in symptoms and physical function."[2] In the nearly 30 years since the first consensus statement, total hip replacements have grown to more than 234,000 procedures each year.[3] With the vast majority of total hip replacement devices coming to market via the 510(k) process, improving incrementally based on the performance of previous generations of devices, millions of patients have experienced positive outcomes and increased access to a life-changing therapy. Total hip replacement is just one way that the reliable, predictable 510(k) pathway has functioned to optimally protect patients and promote innovation in support of public health.

General comments

In General. The Academy's and specialty societies' overarching interest is patient benefit and our comments are directed toward a singular goal of access to safe, effective products for our patients. As surgeons, we witness the benefits of safe, effective, and innovative products and the tragedy of untreated medical problems.

We strongly maintains that, overall, the current 510(k) process works to the benefit of patients and their surgeons by bringing safe, effective products to market, enabling the use of the latest medical technologies for the improvement of patient lives and the public health. Nonetheless, in recent years the 510(k) system has been subject to criticism including our concern about delays and reduced access to new products for patients. The Center for Devices and Radiological Health (CDRH) has proposed more than 70 Working Group reforms, many of which could have serious and significant effects on the ability of physicians to treat their patients with the most effective medical technologies. We are concerned that the reforms, when taken as a whole, could have the effect of impeding the practice of medicine, burdening the doctor-patient relationship, slowing access to the latest medical technologies, and neglecting the inclusion of meaningfully scientific expertise in the 510(k) process.

Process Considerations. Before implementing any of the proposed reforms, we urge FDA to set priorities for reform based on public input, and to then solicit additional stakeholder feedback on detailed, high-priority reforms. The reforms recommended in the August reports are simply too vast and too vague for the agency to move immediately to implementation – formal or informal – without doing serious harm to 510(k) system stakeholders, including, most importantly, patients. For this reason, we urge the agency to prioritize and set out specific, detailed proposals for public comment. Prioritization would better utilize the agency's resources, reduce the regulatory uncertainty that burdens stakeholders, improve the quality and specificity of proposals and responses, and speed the completion of the 510(k) reform effort. Until the agency receives comment on detailed, high-priority proposals through the appropriate legal mechanisms (e.g. notice and comment rulemaking, Good Guidance Practices), FDA ought to avoid informal adoption of any proposed changes. In this regard, AAOS and the specialty societies may support or oppose the general concepts contained in the August report but reserves the right to change our position in response to future specific CDRH proposals that provide the important detail necessary to fully understand the impact of the current, general CDRH recommendations. We have not responded to each CDRH proposal but our silence should not be interpreted to indicate support or opposition.

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[2] Total Hip Replacement. NIH Consensus Statement Online 1994 September 12-14 [October 27, 2010];12(5):1-31.

[3] National Center for Health Statistics, National Hospital Discharge Survey, 2004.

Transparency/Procedural issues. We find that most Agency proposals contained in the CDRH's preliminary reports and recommendations on the 510(k) process and utilizing new science do not provide enough specificity for us to make a determination on their viability or appropriateness.

AAOS has twice commented on FDA transparency initiatives. We appreciate FDA's recent commitment to transparency within the Agency and encourage more transparent processes such as the Agency providing rationales behind decision making processes.

Longer comment periods are needed for proposals and should be expanded to a minimum of 90 days with even longer periods for complex and voluminous proposals. The CDRH will not receive the appropriate input from a variety of stakeholders if stakeholders are not given adequate time to develop comments.

The Practice of Medicine Should be Enhanced, not Impeded, by the 510(k) System
Overall, FDA should not become involved in regulating the practice of medicine and should not take steps that limit the ability of physicians to treat patients in the best, most individualized, fashion.

Promptly Communicating Current or Evolving Thinking to All Affected Parties.
In General. The FDA should make use of more rapid communication tools to convey its current thinking and expectations. Communication of this nature is essential to the maintenance of productive relationships with stakeholders. We strongly support FDA efforts to streamline processes for developing guidance documents and regulation, consistent with the Center's FY 2010 Strategic Priorities. However, the Academy opposes greater use of the "Level 1 – Immediately in Effect" option for guidance documents intended to address a public health concern or lessen the burden on industry. Thoughtful commentary from relevant parties is a critical component of the guidance document development process. Test methods and standard guides that were designed without clinician input could result in guidance documents which fail to consider real world use, and therefore do not adequately evaluate safety and effectiveness. Further, guidance documents lacking clinician contributions can actually contain requirements that are not germane, thereby increasing the regulatory burden and adding barriers to patient access. Finally, limiting the opportunities for interested parties to comment on guidance decreases the transparency of the guidance document process, in direct opposition to the stated goals of the Agency.

FDA should encourage guidance submissions from industry and other constituencies. However, FDA should be required to act on those submissions in a timely manner, recognizing the substantial resources required to development these documents. AAOS has actively participated in guidance document development, yet in our experience at least one document has not been acted upon for nearly seven years.

<u>*Off-Label Use.*</u> We believe that CDRH's proposals regarding off-label rules improperly intrude upon the practice of medicine. FDA has never possessed the authority to regulate the practice of medicine, as the Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §396, expressly prohibits FDA from regulating the practice of medicine.[4] As such, courts have found that physicians may use

[4] *See also*, S. REP. NO. 361, 74th Cong., 1st Sess. 3 (1935) (providing that the FDCA was "not intended as a medical practices act and [did] not interfere with the practice of the healing art.").

legally marketed drugs or devices in any way that they believe, in their professional judgment, will best serve their patients.[5] Indeed, courts have repeatedly recognized the propriety of off-label use.[6] Moreover, many state statutes recognize off-label use in various contexts.[7] Furthermore, "FDA itself recognizes the value and propriety of off-label use," and has reaffirmed their support for off-label use on numerous occasions.[8] In 1997, Congress specifically prohibited FDA intrusion into medical practice with respect to off-label use of devices by amending the FDCA to state, "[n]othing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health-care-practitioner-patient relationship.[9]"

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[5] *See e.g., In re Orthopedic Bone Screw Products Liability Litigation*, MDL No. 1014, 1996 WL 107556, at *3 (E.D. Pa. Mar. 8, 1996) ("the decision whether or not to use a drug for an off-label purpose is a matter of medical judgment, not of regulatory approval") (citation and quotation marks omitted). *See also, Femrite v. Abbott Northwestern Hosp.*, 568 N.W.2d 535, 539n4 (Minn. Ct. App. 1997); *Klein v. Biscup*, 673 N.E.2d 225, 231 (Ohio Ct. App.), appeal denied, 667 N.E.2d 987 (Ohio 1996); and *Piazza v. Myers*, 33 Phila. Co. Rptr. 144, 148 (Pa. C.P. Philadelphia Co. 1997).

[6] *See e.g. Buckman v. Plaintiff's Legal Committee*, 531 U.S. 341 (2001) (For example, with respect to Class III devices, FDA simultaneously maintains the exhaustive PMA and the more limited § 510(k) processes in order to ensure both that medical devices are reasonably safe and effective and that, if the device qualifies under the § 510(k) exception, it is on the market within a relatively short period of time. Similarly, off-label" usage of medical devices (use of a device for some other purpose than that for which it has been approved by FDA) is an accepted and necessary corollary of FDA's mission to regulate in this area without directly interfering with the practice of medicine."

see, e.g., Rhone-Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc., 93 F.3d 511, 514 n.3 (8th Cir.1996); *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1496 (D.C. Cir. 1996); *Ortho Pharm. Corp. v.Cosprophar, Inc.,* 32 F.3d 690, 692 (2d Cir. 1994); *Weaver v. Reagen,* 886 F.2d 194, 198 (8th Cir. 1989);*United States v. An Article of Device . . . Diapulse*, 768 F.2d 826, 832 (7th Cir. 1985); S*chlessing v. United States*, 239 F.2d 885, 886 (9th Cir. 1956); *Washington Legal Found.*, 880 F. Supp. at 28 n.1; *United States v. Evers*, 453 F. Supp. 1141, 1149-50 (M.D. Ala. 1978), *aff'd*, 643 F.2d 1043, 1052-53 (5th Cir. 1981); *FTC v. Simeon Management Corp.*, 391 F. Supp. 697, 706 (N.D. Cal. 1975), *aff'd*, 532 F.2d 708 (9th Cir. 1976); *Upjohn Co. v. MacMurdo*, 562 So. 2d 680, 683 (Fla. 1990); *Jones v. Petland Orlando Store*, 622 So. 2d 1114, 1115 (Fla. Dist. Ct. App. 1993); *Haynes v. Baton Rouge Gen. Hosp.*, 298 So. 2d 149, 153 (La. Ct. App. 1974), *writ denied*, 302 So. 2d 33 (La. 1974); Peter Hutt, *Regulation of the Practice of Medicine Under the Pure Food & Drug Laws*, 33 ASS'N FOOD & DRUG OFFICIALS Q. BULL. 7-11 (1969).

[7] *Id* at 76-77, referring to FDA Drug Bulletin 4-5 (1982) (cited in 59 Fed. Reg. 59,820, 59,821 (Nov. 18, 1994), and *citing. see, e.g.,* ALA. CODE §§ 27-1-10.1(a), (c) (Supp. 1997) (Alabama); CAL. INS. CODE § 10123.195(a) (West Supp. 1997) (California); CAL. HEALTH & SAFETY CODE § 1367.21(a) (West Supp. 1997) (California); CONN. GEN. STAT. §§ 38a-492b(a), 38a-518b(a) (1995) (Connecticut); FLA. STAT. ANN. § 627.4239 (West 1996) (Florida); GA. CODE ANN. § 33-53-2 (Michie 1993 & Supp. 1997) (Georgia); 1992 ILL. LAWS 980 §§ 1-2 (1992, uncodified) (available on LEXIS, 1992 Ill. ALS 980) (Illinois); 5 ILL. COMP. STAT. § 375/6.4 (West 1993 & Supp. 1997) (Illinois); 215 ILL. COMP. STAT. §§ 5/370r, 125/4-6.3 (West 1993 & Supp. 1997) Illinois); IND. CODE ANN. § 27-8-20-7 (Burns 1993 & Supp. 1997) (Indiana); LA. REV. STAT. ANN. § 22:215.18 (West) (Louisiana); MD. CODE ANN., INS., § 15-804 (1997) (Maryland); MASS. GEN. LAWS ANN. ch. 175 §§ 47K-L, 47O-P; ch. 176A §§ 8N, 8Q; ch. 176G § 4G (West Supp. 1996) (Massachusetts); MICH. COMP. LAWS ANN. §§ 500.3406e, 500.3616a (West 1996) (Michigan); N.C. GEN. STAT. §§ 58-67-78, 58-51-59 (Supp. 1996) (North Carolina); N.D. CENT. CODE § 26.1-36-06.1 (1997) (North Dakota); OHIO REV. CODE ANN. § 1751.66 (Banks-Baldwin 1997) (Ohio); OKLA. STAT. ANN. tit. 63 §§ 1-2604, 1-2605 (West 1996) (Oklahoma); R.I. GEN. LAWS §§ 27-55-2, 27-55-3 (1996) (Rhode Island); S.C. CODE ANN. § 38-71-275 (Law. Co-op. 1996) (South Carolina); TENN. CODE ANN. § 56-7-2352 (1997) (Tennessee); UTAH CODE ANN. § 26-18-105(7) (Supp. 1997) (Utah); VA. CODE ANN. § 38.2-3407.5 (Michie 1997) (Virginia).

[8] *Id* at 77, *citing* 59 Fed. Reg. at 59,821. *Accord, e.g.,* 52 Fed. Reg. 8798, 8803 (Mar. 19, 1987) (reaffirming legality of off-label use); 48 Fed. Reg. 26,720, 26,733 (June 9, 1983) (reaffirming legality of off-label use); 40 Fed. Reg. 15,392, 15,393-94 (Apr. 7, 1975) (reaffirming legality of off-label use); 37 Fed. Reg. 16,503, 16,503-04 (Aug. 15, 1972) ("[o]nce [an approved] new drug is in a local pharmacy . . . the physician may, as part of the practice of medicine, lawfully . . . vary the conditions of use from those approved"); FOOD AND DRUG ADMIN., COMPLIANCE
PROGRAM GUIDANCE MANUAL No. 7382.900 pt. I, at 7 (1992) ("physicians may use devices for off-label uses (This is considered within the practice of medicine)").

[9] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 214, 111 Stat. at 2348 (codified at 21 U.S.C. § 396 (FDCA § 906)).

These restrictions make clear that FDA does not have the power to interfere with the practice of medicine, and thus any change to the 510(k) system must not limit physicians' ability to use medical devices as they see fit in the best interests of patients. We strongly disagree with the recommendation that FDA seek the statutory authority to consider off-label use when determining intended use. FDA currently has more than adequate enforcement powers relating to off-label matters. Any additional authority could inappropriately obstruct the practice of medicine, as physicians rely on the ability to use approved devices to treat conditions that are closely related to an indicated condition. New and innovative medical developments that may advance patient care are constantly emerging in an era when technological developments may rapidly outpace traditional educational opportunities for discussion and the regulatory review framework. It is not uncommon for some uses of medical products to become standard of care in the practice of medicine before manufacturers seek approval or clearance of the labeled indications for use for a particular product.

"Indications for Use" and "Intended Use". Similarly, AAOS and the specialty societies do not support CDRH's recommendation to combine the terms "indications for use" and "intended use." First, "intended use" is a statutory term, *see e.g.* 21 U.S.C. §360(c)(i)(a)(A), and that statutory language must be honored. The phrase "indications for use" is found in regulations, not statute; and the combination of these terms would improperly blur the distinction between these terms. The combination of these terms would require FDA to amend multiple prior regulations and guidance to reflect the new standards and terminology.

Second, combining these terms would impact the practice of medicine and could limit surgeons' access to medical technologies that could improve patient care. For example: Under today's rules, forceps might have a proposed labeling claim saying its intended use was "to grasp and hold objects or tissue" and thus surgeons could apply its use to a wide array of disease states and stay within the general labeling. However, to add "indications for use" for a specific type of tissue or in a particular procedure such as heart surgery to the labeling would perhaps trigger new review cycles or otherwise unnecessarily add to the regulatory burden on the agency and other stakeholders. Combining these terms could allow reviewers to interpret this guidance such that the company would be forced to demonstrate a forceps's clinical benefit as a bone or heart device, rather than simply the more straightforward, yet broad "intended use." This potential for misinterpretation will burden manufacturers and FDA, but ultimately it will be surgeons and patients who suffer if devices are delayed or unavailable due to new regulatory requirements. Forceps are but one example of devices that are essential to a surgeon's practice of medicine, whose access could be limited if manufacturers were forced to study and prove all indications. Rather, the determination of the appropriate specific use of the product belongs in the hands and judgment of the experienced physician. We fear that combining the terms "indications for use" and "intended use" could have significant unintended consequences for the practice of medicine and opposes combining the terms.

Third, the combination of these terms may result in many products being needlessly forced into new PMAs, which would slow speed to market without benefiting patient safety. As such, the combination of these terms will lead to delays in product reviews and confusion as to when filings are required. Rather than combining these terms, we encourage FDA to, through Administrative Procedures Act ("APA") rulemaking, explicitly define and distinguish the terms "indications for use" and "intended use" based on current statutory definitions and existing concepts. These definitions should clarify but not change the existing meaning of these terms.

Rescission Authority. We support FDA's authority to rescind specific 510(k)s due to safety concerns or obtained by fraud when necessary to protect patients. Fundamentally and obviously, fraudulent conduct must not be permitted. However, we do not support an expansion of FDA's rescission authority to a 510(k) for reasons other than fraud and safety concerns, as such expanded authority would call into question the legal marketing status of each device that had subsequently relied on the rescinded device as a predicate, even in the absence of evidence to suggest subsequent devices are subject to the same inadequacies as the rescinded predicate device. AAOS and the specialty societies believe subsequent 510(k)s that utilized the rescinded product as a predicate should not be affected unless FDA finds that the subsequent, related devices present a significant public health risk under a section 360(e)-type process or that they also involved fraudulent conduct by the applicant. Stated simply, the rescission of one product ought not, necessarily, impact related products without further showing of fraud. Otherwise, physicians and their patients risk losing access to essential products without justification for the harm caused to patient health and the practice of medicine

The FDCA provides FDA with numerous efficient means to remove unsafe or violative devices from the market:

- 21 USC §513(i) sets forth how FDA can legally refuse to permit the use of a fraudulent 510(k);
- 21 U.S.C. §516 authorizes FDA to ban medical devices in situations of substantial deception or unreasonable and substantial risk of illness or injury, where banned devices can no longer be legally marketed and can therefore not be cited as a predicate device;
- 21 U.S.C. §518 provides FDA the authority to issue a mandatory recall;
- 21 U.S.C. §513(e) authorizes FDA to reclassify a device based on new information, including reassessment of past information in the administrative record; FDA may obtain a court order for product seizure;
- 21 U.S.C. §360(e) provides a process for removing devices that present a significant public health risk;
- 21 U.S.C. §§331-334 gives the agency the power to seize violative product, utilize all equitable relief avenues and bring civil and criminal enforcement action; and

The rescission of a 510(k) clearance or recall of a medical device may not necessitate an immediate change in patient treatment, as 510(k) rescission or device recall does not inevitably mean that the device presents a risk to every patient. Patient safety must be the first priority, and sometimes it is safer for the patient, particularly when dealing with implantable devices, to leave the device in place and avoid the risks associated with explanation of the device and implantation of an alternative. In cases of implanted devices, surgeons play a critical role in the identification of implant failure, the appropriate use of resources to address medical concerns related to its failure, and the education of patients on the risks and benefits of the implanted device and of revision surgery. We strongly believes that physicians and patients should have the final say in whether a rescission or recall presents a significant patient safety risk to justify a change in patient treatment, as this too is part of the practice of medicine over which FDA does not have authority. Surgeons must have the ability and flexibility to act in the patient's best interest. As is true in instances of recall, where a 510(k) clearance has been rescinded, surgeons should consult with patients and consider the facts and circumstances unique to each patient in order to determine the best course of treatment in light of FDA's determination regarding the product.

Patients and Physicians Benefit from a Consistent, Balanced 510(k) System

Postmarket Surveillance. The Food and Drug Administration Amendments Act of 2007 provided the FDA with new postmarket authorities including an expansion of 522 or postmarket surveillance studies and a mandate to institute a unique device identification (UDI) system. While the CDRH has implemented a few new 522 studies, the CDRH has not yet issued a proposed rule for a UDI system. Taken together with an electronic health record, the UDI system will greatly enhance the postmarket capabilities of the CDRH. We suggest that the FDA implement the authorities already granted them by Congress rather than seeking additional authorities at this time.

AAOS and the specialty societies do not support the recommendation for FDA to "potentially seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices." Such additional authority is unnecessary, as FDA already has the ability to issue Section 522 orders and to include postmarket studies in premarket special controls through section 360(a)(1)(B). Furthermore, there is no evidence to show that additional postmarket surveillance would add value to the 510(k) process.

Perhaps more importantly for our members, any unjustified additional postmarket surveillance requirements threaten to burden surgeons and any additional requirements need to take this burden into account. Additional postmarket surveillance requirements force surgeons to spend more time on the administrative obligations during clinic practice, and divert them from essential patient care. Patients' access to their surgeons is already limited by many tasks not directly related to the provision of care. Additional administrative duties mean less time to serve patients, which either results in a reduced number or duration of appointments each day**.** In our view, this is not a financial issue that can be remedied through patient or physician remuneration. The most valuable resource the surgeon has is time and requiring additional time be spent on postmarket surveillance inexorably leads to less time for patients.

Before instituting any new postmarket surveillance systems, FDA should first determine whether and how existing postmarket surveillance programs, as well as public and private initiatives, have improved public health**.** Absent evidence of how this additional authority would significantly improve quality of care, we cannot agree that the burden such requirements would place on surgeons is justified by the benefit.

The goal of any postmarket surveillance requirements be the prevention of patient harm and minimization of health systems errors. Any postmarket surveillance system should foster open dialogue and reporting and we believe systems with punitive undertones would defeat this purpose. Any additional postmarket surveillance requirements should be clearly defined, with strictly enforced parameters for defining when such action is necessary to evaluate the safety and effectiveness of a device.

*510(k) Databases***.** We support the development of a publicly available, easily searchable 510(k) database, including summaries, regularly updated labeling, and current ownership information. The existence of this data will enable surgeons and patients to access materials that support shared decision-making, particularly in an environment of direct-to-consumer advertising. It will also facilitate the identification of device information prior to revision surgery and provide a mechanism by which surgeons can readily locate manufacturers to acquire replacement parts and instrumentation for these procedures.

The Academy and specialty societies strongly urge FDA to not just create this database, but to maintain it such that it reflects the most up-to-date information at all times. Providing a single location for this data will strengthen FDA's relationship with consumers and support the doctor-patient relationship.

De novo process. We agree that substantive changes are necessary to make the de novo process more efficient and effective. The Agency should completely rework this process so that it is predictable, transparent, and is a viable pathway to bring novel therapeutic options to patients expeditiously.

Reviewer expertise and experience. The Academy supports the enhancement of efforts to recruit, retain, train, and increase professional development experiences of CDRH personnel. Specialty societies represented by our members have served as faculty in educational sessions for FDA staff for at least a decade, and are ready and willing to continue to do so.

Collaboration with specialty societies. FDA should continue to routinely communicate with medical specialty associations, their leadership and staff, regarding physician and specialty specific issues. Medical specialty organizations are well equipped to work with regulatory agencies, such as FDA, on mutual issues of importance and can quickly disseminate information to their members and obtain important and timely feedback.

*Metrics***.** We support the development of program metrics to continuously assess the quality, consistency, and effectiveness of the 510(k) program. Periodic audits should occur and the Agency should incorporate the learned knowledge into continued improvement of the 510(k) program.

Guidance Document Development. AAOS and the specialty societies acknowledge the success of the utilization and development of FDA guidance documents. These documents assist in enhancing predictability for manufacturers, FDA reviewers, and other stakeholders in the development of pre-market device and notification submissions, and expedite the review process. Guidance documents assist in the standardization of FDA policy and interpretation. Additionally, guidance documents are often used as special controls to support a down-classification.

The Academy agrees with the recommendations of the 2007 Science Board that the CDRH should develop and spend more time on guidance documents, standards and other written publications, and archiving and retrieval systems, with written precedent files, so that once a decision is reached, subsequent reviewers are informed of the previous decisions. AAOS has commented repeatedly over the last few years protesting the decreasing rate of guidance document publication following the establishment of the 2002 Medical Device User Fee Act (MDUFMA) performance goals.

Delays in published guidance documents are of significant concern as it generally means that new therapeutics will take longer to reach patients. While there are differing priorities within FDA divisions, offices, and centers, we suggest that the Agency devote considerably more resources to the development of needed guidance documents. In order to fully implement many of the CDRH's 510(k) proposals, the Center will need to develop many new guidance documents, in addition to the backlog of guidance document development that currently exists.

Physicians Rely on the Latest Medical Technologies to Serve Their Patients

In General. Patients and their physicians need the most recent, innovative products to address health problems. Without access to the latest medical technologies, U.S. surgeons will be under-equipped

to respond to their patients' needs. AAOS and the specialty societies emphasize that the 510(k) system directly affects our members' ability to provide state-of-the-art care for their patients. Surgeons' use of new medical devices benefit patients by, for example, addressing unmet clinical needs, reducing healing time (injectable scaffolds), increasing post-op mobility (fixed angle devices), decreasing implant sensitivity (oxinium and zirconia nitrite coatings), and improving pain management (nerve stimulators). Increasingly, medical innovation is essential to the practice of medicine as the latest medical technologies can – and do – dramatically improve patient treatment and outcomes.

Physicians also play an essential role in driving innovation. Surgeons identify and raise awareness of specific patient and public health needs for new innovation. In the course of their practice and their time with patients they learn of unmet health needs, identify needed engineering and technological modifications to products, and identify new procedures, techniques, and applications of products. They also advise on the creation, use, and setting of high performance and clinical standards for medical devices through participation in the development of consensus standards, review boards, and advisory councils

Multiple and Split Predicates. We urge CDRH to continue to allow the use of split and multiple predicates. Use of split and multiple predicates fosters innovation that is essential to patient care. Combining or building upon already proven medical technologies by using split predicates or multiple predicates leads to better, more efficiently delivered patient care. Correspondingly, restricting use of split and multiple predicates will slow innovation, which negatively impacts patient care, and increases costs to all stakeholders. Disallowing the use of split or more than five predicates could lead to unnecessary PMAs and *de novo* requests. Lacking access to FDA's data substantiating their claim of a correlation between 5 or more predicates and a greater mean number of adverse event reports, we are unable to assess the actual risk represented by these devices. Adverse events are frequently multi-factorial in origin. Failing independent evaluation of this data, we are cannot establish a causal relationship between the use of more than five predicates and adverse event rates. We urge FDA to make this data public so that surgeons may make informed decisions when selecting devices. Additionally, split predicates enable robust product reviews, as information from different areas is considered in the submission examination.

We recognize that some improvements for administrative efficiency and predictability might be warranted and such could likely be accomplished through guidance. However, FDA has no statutory or regulatory basis to prohibit or limit the use of split predicates. Similarly, to disallow use of multiple predicates, FDA would need to amend CDRH's 1986 guidance[10] allowing multiple predicates.

Class IIb. We do not support the creation of a Class IIb, at this time. First, we question whether FDA has the authority to create the proposed class. Congress has authorized the use of special controls for Class II devices, and these special controls should be applies on a case-by-case basis. Congress has not authorized CDRH to establish another class, and FDA does not have the authority to do so because, regardless of how Class IIb is described, the result would be to create a broad, new set of requirements that apply across multiple products, and that is the meaning of a class. Without a change in the statute to create and define a new class, CDRH cannot move forward with this recommendation. Furthermore, FDA has presented no safety data to show that there is a problem

[10] *Guidance on the Center for Devices and Radiological Health's Premarket Notification Program* (*Blue Book Memo. #K86-3*) (June 30, 1986).

for a group of 510(k) products which justifies the additional proposed "Class IIb" requirements. This is particularly true for orthopedic devices. The research presented by Dr. Maisel and Professor Hall at the July IOM meeting demonstrates that, overall, orthopedic devices present a low risk for safety related product recalls. Simply assuming that implantable devices require more burdensome premarket requirements is unfounded in science and results in irresponsible policy. We urge the agency to set forth the data which supports the recommendation for this new "Class IIb" so that stakeholders can review and respond to the specific concern FDA seeks to address with this proposal.

Second, should FDA seek to create a Class IIb, we fear that this could lead to the tendency to "up classify" devices in to the PMA-like "Class IIb" requirements and to place products going through the de novo process automatically into Class IIb. This means products that do not pose a specific risk would unnecessarily be delayed in getting to market, which results in surgeons having limited access to the latest medical technologies. Physicians and patients need to have access to innovative medical devices as soon as possible, especially where there is no product-specific, evidenced safety risk which justifies delay. Class-wide, automatic requirements could also have long-term negative consequences for patients suffering from the medical conditions that certain new "Class IIb" devices address. Class IIb, as proposed by FDA, will significantly increase the time and burden to bring new products to market. These additional costs resulting from the proposed new classification will stall innovation in those product lines, leading to fewer devices brought to market for certain medical conditions. We are particularly concerned about orthopedic products being pushed into the new proposed Class IIb and thus reducing innovation and depriving our patients of valuable new therapies. Rather than establishing a new, broad "class," we encourage FDA to continue to apply special controls to protect the public health on a case-by-case basis.

Science, Data and Medical Expertise are Essential to the 510(k) System

Consensus Standards: As surgeons, we hold patient safety and benefit in the highest regard, and thus stand behind the importance of consensus standards ("standards") which embody the highest concern for safety. Currently, clinicians, researchers and practicing surgeons contribute to the development of standards by participating in national and international standards development organizations, e.g. American Society for Testing and Materials, International ("ASTM"). We firmly believe that the contributions of medical experts to the development of standards for medical devices ensure the protection of our patients' vital interests. Medical experts provide "real-world" insight on how the devices will actually be used in patients, which improve standards and thus ultimately improve patient outcomes. Moreover, as technology and medical knowledge advance, standards must also evolve and medical experts are relied upon to provide assistance in the development of appropriate standards for these emerging medical devices. We support the continual, ongoing involvement of medical experts in monitoring national and international standards which are essential to the practice of surgeons for clinical relevance, revising them as peer reviewed evidence from clinical, scientific and technological information warrant.

Any reform of the 510(k) program must ensure that medical experts have a strong voice in the development of consensus standards. By changing or failing to reference these standards, or by altering the forum used to develop standards, FDA threatens to shut out medical experts from the standards development process. Such a change would greatly disserve patients, whose interests are represented by medical experts participating in the standards process, and harm surgeons who rely on workable, consensus-based standards in order to provide the best possible patient care. Furthermore, FDA's failure to obtain or rely on input from medical experts in consensus standards

could greatly harm innovation. Because manufactures would not have the benefit of early input from physicians and surgeons as provided through the standards development process, companies will either need to seek out clinician input in advance from alternative sources – thus adding costs and possible delay – or await clinician input from FDA – which could mean significant late-stage costs and delays. In short, early clinician input helps patients and physicians, and improves innovation. We urge CDRH to preserve the essential role of medical experts in the development of consensus standards.

Center Science Council. We support the establishment of a transparent, expert-lead Center Science Council. This council must include external experts such as practicing physicians. We are, however, concerned that due to rigid application of conflict of interest rules the Center Science Council could end up staffed with inexperienced scientists rather than science experts who often have been involved in numerous roles throughout the medical device community. It would be unfortunate, inefficient, and potentially harmful to the public health should the Center Science Council fail to be appropriately staffed with well-informed experts.

FDA must be mindful of the many administrative law requirements at issue in forming and operating a proposed panel like the Center Science Council. FDA should make public, with an opportunity for stakeholder input, its initial proposals for the Council's roles, responsibilities and processes. These administrative law requirements are especially important when considering the potential role(s) of the Center Science Council in product reviews and scientific debates. Additionally, in light of the potential legal and administrative costs in setting up and operating the Center Science Council, at a time when the U.S. Government is especially strapped for resources, we urge FDA to calculate the costs before proceeding so that, if established, the Center will be funded at the level required to maximize its potential value.

Experts via social media. We encourage FDA to establish access to a wide range of experts, including clinicians, surgeons and diagnostic experts who can speak to the "real-world" application of medicinal devices. While we commend FDA for "thinking outside the box" in trying to guarantee the agency has access to these experts, AAOS is concerned that CDRH may not have fully contemplated the potential for confidentiality, conflict of interest, and FACA issues inherent in using social media. If a web-based expert panel were to be used, to be consistent with FDA's transparency initiative, we would hope the agency would make the selection and names of external experts (including qualifications) available on the FDA website.

AAOS and the specialty societies are very interested in helping serve as experts to FDA in more formalized and effective ways than currently exist. We encourage FDA to look for ways maintain communication with the pools of potential panelists. More active engagement with surgeons stands to make the 510(k) system more safe and effective, a result which improves the public health. AAOS is ready and able to provide experts to FDA to fill this important role.

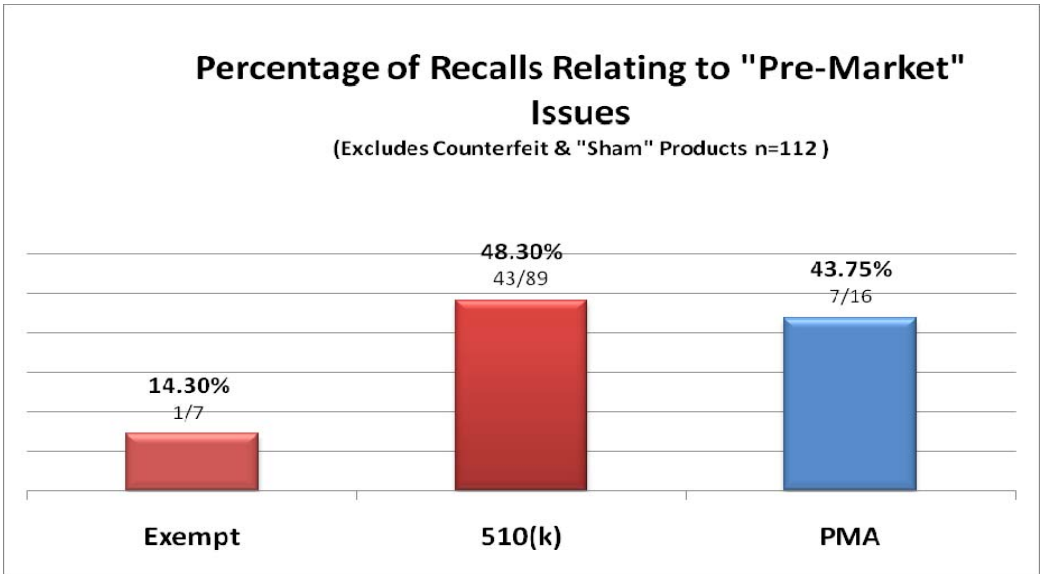
Evidenced-based reforms. We strongly support using evidence to determine what changes might be needed to the 510(k) system. Making changes other than on an evidence-based method risks changes that adversely affect patients. For this reason, we urge the FDA consider the 510(k) system using Class I recall data in any potential changes.

Professor Ralph Hall from the University of Minnesota Law School studied FDA Class I recalls of medical devices between 2005 and 2009. There were 118 unique recalls in that category and of those,

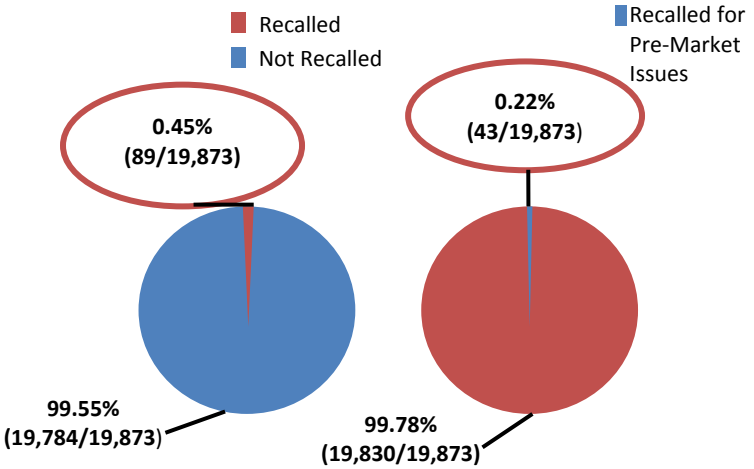
roughly 55 percent were associated with post approval or post clearance quality system issues rather than a lack of premarket clinical data. Forty-five percent of the recalls due "pre-market" issues mostly involved design and software design problems. *Figures below from R. Hall presentation at IOM Meeting 3: Public Health and Effectiveness of the 510(k) Clearance Process, July 28, 2010.*

Primary Reason for Recall	PMA	510K	Class 1	Other or Unknown	TOTAL
Manufacturing	6	31	2	1	**40**
Labeling Error	0	4	0	0	**4**
Design Issue	6	25	1	0	**32**
Software Design	1	9	0	0	**10**
Software Manuf. Failure	0	2	0	0	**2**
Supplier Issue	2	5	0	0	**7**
Failure to Identify Clinical Risk	0	0	0	0	**0**
Failure to Warn/Inadequate Instructions	0	8	0	0	**8**
Missing Parts	0	0	0	0	**0**
Sterilization	1	4	2	0	**7**
Regulatory Violation	0	1	1	0	**2**
Packaging/Handling	0	0	0	0	**0**
Other (Counterfeit, Sham)	0	6	0	0	**6**

Hall's study shows that CDRH should concentrate on QSR systems and not burden innovation with premarket requirements that do not contribute to patient safety. Simply put, there is no evidence that additional clinical studies testing medical devices in humans would have prevented the pre-market problems behind most serious recalls. Suggestions that there should be more burdensome premarket clinical testing or more burdensome review requirements lack an evidentiary basis. Unless FDA has – and publicly publishes – new data that convincing demonstrates that there is a patient need for increased premarket burden, CDRH must be very careful not to regulate based on anecdote and unsubstantiated fear.



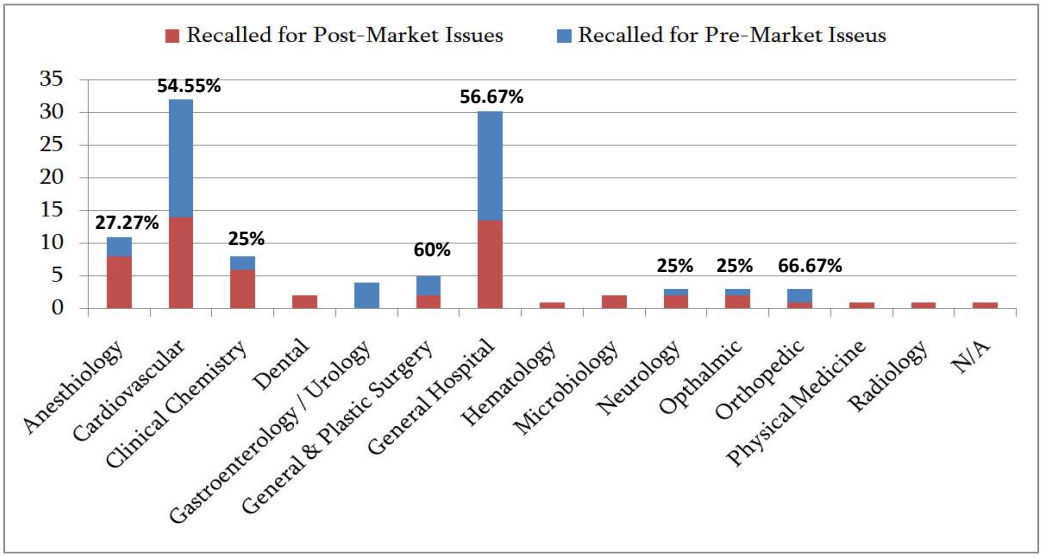
Moreover, Hall's data shows that, based on Class I (safety) recalls, FDA has an excellent record, where approximately 99.8% of product submissions did not experience a Class I recall in a five year period.



Total 510(k) Submissions 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**

Furthermore, of the approximately **0.22%** of devices that were subject to a Class I recall, a rare few were for orthopedic products. Indeed, many product types have few or no recalls; there has been a concentration of recalls in AEDs and infusion pumps.

Recalls by Medical Specialty, Percentage of Recalls for Pre-Market Issues
n = 112



A study by William Maisel also supports conclusion that the vast majority of the time the 510(k) system works to bring and keep safe and effective products in the market. When recalls do occur, they most often involve manufacturing and device design issues that would not be impacted by additional pre-market clinical data, and rarely involve orthopedic products. At the July 28, 2010 meeting of the Institute of Medicine's committee reviewing the public health effectiveness of the FDA 510(k) clearance process, Dr. Maisel summarized the key findings of his study as follows:

1. More than 3000 devices are cleared for marketing each year under new 510(k)s. Overall, there have been more than 48,000 510(k)s since 1996.
2. Recalls affect 510(k) devices 400-500 times annually.
3. The annual rate of recall for 510(k) products is ~1.3-1.5% per year for the first 4 years post clearance; the rate falls to ~1.0% for post-market years 5-6.
4. Manufacturing process and device design issues are the most common causes cited for 510(k) recalls.
5. A large number of predicates, special 510(k)s, 3rd party reviews, and life-sustaining devices are associated with a higher rate of recall.

These studies shows that orthopedic devices overall have an excellent safety record. As such, additional pre-market burdens on orthopedic products offer little benefit but substantial risk of reduced availability of innovative new products. We support evidence-based reforms, and encourage the FDA to consider whether the Hall and Maisel data supports each proposed change to the 510(k) system.

Conclusion

AAOS and the undersigned orthopaedic specialty societies support regulatory systems that provide safe, efficacious products for our patients. We appreciate this opportunity to share our comments on the Task Force proposals and will look forward to future opportunities to engage with FDA on improving the 510(k) process.

Sincerely,

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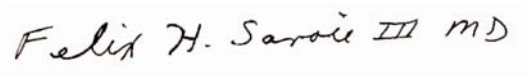

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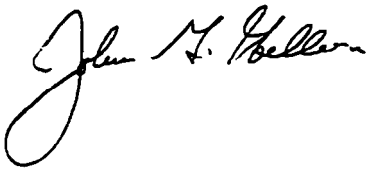

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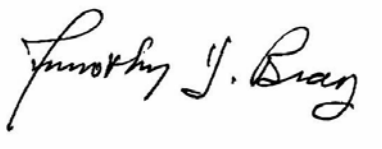

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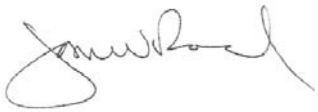

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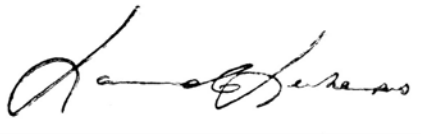
Ruth Jackson Orthopaedic Society



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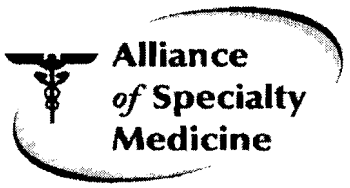
Alliance of Specialty Medicine, et al. – Comment (posted 11/09/10)

FDA-2010-N-0348-0076



Sound Policy. Quality Care.

Rec'd 11/8/2010

November 4, 2010

Margaret A. Hamburg, MD
FDA Commissioner
Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. FDA-2010-N-0348: Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations, and Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability; Request for Comments

Dear Commissioner Hamburg:

The Alliance of Specialty Medicine (Alliance), a coalition of 10 national medical specialty societies representing more than 100,000 physicians and surgeons, is dedicated to the development of sound federal health care policy that fosters patient access to the highest quality specialty care. The Alliance commends the 510(k) Working Group and Task Force for their efforts, and thanks Director Shuren and the FDA for soliciting stakeholder comment and town hall feedback.

General comments

In General. The Alliance's overarching interest is patient benefit and our comments are directed toward our primary goal of assuring access to safe, effective products for our patients. As specialists, we witness the benefits of safe, effective, and innovative products and the misfortunes of untreated medical problems.

The Alliance strongly maintains that overall, the current 510(k) process works to the benefit of patients and their physicians by allowing safe, effective products to enter the market, enabling the use of the latest medical technologies to improve patient lives and the public health. Nonetheless, in recent years the 510(k) system has been subject to criticism including our concern about delays and reduced access to new products for patients. The Center for Devices and Radiological Health (CDRH) has proposed more than 70 Working Group reforms, many of which could have serious and significant effects on the ability of physicians to treat their patients with the most effective medical technologies. We are concerned that the reforms, when taken as a whole, could have the effect of impeding the practice of medicine, burdening the doctor-patient relationship, slowing access to the latest medical technologies, and limiting the inclusion of meaningful scientific expertise in the 510(k) process.

Process Considerations. Before implementing any of the proposed reforms, the Alliance urges FDA to set priorities for reform based on public input, and to then solicit additional stakeholder feedback on detailed, high-priority reforms. The reforms recommended in the August reports are simply too vast and too vague

FDA 2010-N-0348

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for the agency to move immediately to implementation – formal or informal – without doing serious harm to 510(k) system stakeholders, including, most importantly, patients. For this reason, we urge the Agency to prioritize and set out specific, detailed proposals for public comment. Prioritization would better utilize the Agency's resources, reduce the regulatory uncertainty that burdens stakeholders, improve the quality and specificity of proposals and responses, and speed the completion of the 510(k) reform effort. Until the Agency receives comments on detailed, high-priority proposals through the appropriate legal mechanisms (e.g. notice and comment rulemaking, Good Guidance Practices), the FDA ought to avoid "informal" adoption of any proposed changes. In this regard, the Alliance may support or oppose the general concepts contained in the August report but reserves the right to change our position in response to future specific CDRH proposals that provide the important detail necessary to fully understand the impact of the current, general CDRH recommendations. Likewise, the Alliance will not respond to each CDRH proposal and our silence on specific recommendations, should not be interpreted to indicate our support or opposition.

Transparency/Procedural issues. The Alliance finds that most Agency proposals contained in the CDRH's preliminary reports and recommendations on the 510(k) process and utilizing new science do not provide enough specificity for us to make a determination of their viability or appropriateness.

The Alliance has twice commented on FDA transparency initiatives. We appreciate the FDA's recent commitment to transparency within the Agency and encourage more transparent processes such as providing Agency rationales behind decision- making processes.

Longer comment periods are needed for proposals and should be expanded to a minimum of 90 days with even longer periods for complex and voluminous proposals. The CDRH will not receive the appropriate input from a variety of stakeholders if stakeholders are not given adequate time to develop comments.

The Practice of Medicine Should be Enhanced, not Impeded by the 510(k) System

Overall, FDA should not become involved in regulating the practice of medicine and should not take steps that limit the ability of physicians to treat patients in the best, most individualized, fashion.

Promptly Communicating Current or Evolving Thinking to All Affected Parties

The Alliance agrees that the FDA should make use of more rapid communication tools to convey its current thinking and expectations. Communication of this nature is essential to the maintenance of productive relationships with stakeholders. We strongly support efforts to streamline FDA processes for developing guidance documents and regulation, consistent with the Center's FY 2010 Strategic Priorities. However, the Alliance opposes greater use of the "Level 1 – Immediately in Effect" option for guidance documents intended to address a public health concern or lessen the burden on industry. Thoughtful commentary from relevant parties is a critical component of the guidance document development process. Test methods and standard guides that are designed without clinician input could result in guidance documents which fail to consider "real world" use, and therefore do not adequately evaluate safety and effectiveness. Further, guidance documents lacking clinician contributions can actually contain requirements that are not germane, thereby increasing the regulatory burden and adding barriers to patient access. Finally, limiting the opportunities for interested parties to comment on guidance documents decreases the transparency of the guidance document process, in direct opposition to the stated goals of the Agency.

The FDA should encourage guidance document submissions from industry and other constituencies. However, the FDA should be required to act on those submissions in a timely manner, recognizing the substantial resources required to develop these documents.

Off-Label Use. The Alliance believes that CDRH's proposals regarding off-label rules improperly intrude upon the practice of medicine. The FDA has never had the authority to regulate the practice of medicine,

as the Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §396, expressly prohibits FDA from regulating the practice of medicine.[1] As such, courts have found that physicians may use legally marketed drugs or devices in any way that they believe, in their professional judgment, will best serve their patients.[2] Indeed, courts have repeatedly recognized the propriety of off-label use.[3] Many state statutes recognize off-label use in various contexts.[4] Moreover, "the FDA itself recognizes the value and propriety of off-label use," and has reaffirmed their support for off-label use on numerous occasions.[5] In 1997, Congress specifically prohibited FDA intrusion into medical practice with respect to off-label use of devices by amending the FDCA to state, "[n]othing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health-care-practitioner-patient relationship.[6]"

These restrictions make clear that the FDA does not have the power to interfere with the practice of medicine, and thus any change to the 510(k) system must not limit physicians' ability to use medical devices

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[1] *See also*, S. REP. NO. 361, 74th Cong., 1st Sess. 3 (1935) (providing that the FDCA was "not intended as a medical practices act and [did] not interfere with the practice of the healing art.").

[2] *See e.g., In re Orthopedic Bone Screw Products Liability Litigation*, MDL No. 1014, 1996 WL 107556, at *3 (E.D. Pa. Mar. 8, 1996) ("the decision whether or not to use a drug for an off-label purpose is a matter of medical judgment, not of regulatory approval") (citation and quotation marks omitted). *See also, Femrite v. Abbott Northwestern Hosp.*, 568 N.W.2d 535, 539n4 (Minn. Ct. App. 1997); *Klein v. Biscup*, 673 N.E.2d 225, 231 (Ohio Ct. App.), appeal denied, 667 N.E.2d 987 (Ohio 1996); and *Piazza v. Myers*, 33 Phila. Co. Rptr. 144, 148 (Pa. C.P. Philadelphia Co. 1997).

[3] *See e.g. Buckman v. Plaintiff's Legal Committee*, 531 U.S. 341 (2001) (For example, with respect to Class III devices, the FDA simultaneously maintains the exhaustive PMA and the more limited § 510(k) processes in order to ensure both that medical devices are reasonably safe and effective and that, if the device qualifies under the § 510(k) exception, it is on the market within a relatively short period of time. Similarly, off-label" usage of medical devices (use of a device for some other purpose than that for which it has been approved by the FDA) is an accepted and necessary corollary of the FDA's mission to regulate in this area without directly interfering with the practice of medicine."

see, e.g., Rhone-Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc., 93 F.3d 511, 514 n.3 (8th Cir.1996); *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1496 (D.C. Cir. 1996); *Ortho Pharm. Corp. v.Cosprophar, Inc.,* 32 F.3d 690, 692 (2d Cir. 1994); *Weaver v. Reagen,* 886 F.2d 194, 198 (8th Cir. 1989);*United States v. An Article of Device . . . Diapulse*, 768 F.2d 826, 832 (7th Cir. 1985); S*chlessing v. United States*, 239 F.2d 885, 886 (9th Cir. 1956); *Washington Legal Found.*, 880 F. Supp. at 28 n.1; *United States v. Evers*, 453 F. Supp. 1141, 1149-50 (M.D. Ala. 1978), *aff'd*, 643 F.2d 1043, 1052-53 (5th Cir. 1981); *FTC v. Simeon Management Corp.*, 391 F. Supp. 697, 706 (N.D. Cal. 1975), *aff'd*, 532 F.2d 708 (9th Cir. 1976); *Upjohn Co. v. MacMurdo*, 562 So. 2d 680, 683 (Fla. 1990); *Jones v. Petland Orlando Store*, 622 So. 2d 1114, 1115 (Fla. Dist. Ct. App. 1993); *Haynes v. Baton Rouge Gen. Hosp.*, 298 So. 2d 149, 153 (La. Ct. App. 1974), *writ denied*, 302 So. 2d 33 (La. 1974); Peter Hutt, *Regulation of the Practice of Medicine Under the Pure Food & Drug Laws*, 33 ASS'N FOOD & DRUG OFFICIALS Q. BULL. 7-11 (1969).

[4] *Id* at 76-77, referring to FDA Drug Bulletin 4-5 (1982) (cited in 59 Fed. Reg. 59,820, 59,821 (Nov. 18, 1994), and *citing. see, e.g.,* ALA. CODE §§ 27-1-10.1(a), (c) (Supp. 1997) (Alabama); CAL. INS. CODE § 10123.195(a) (West Supp. 1997) (California); CAL. HEALTH & SAFETY CODE § 1367.21(a) (West Supp. 1997) (California); CONN. GEN. STAT. §§ 38a-492b(a), 38a-518b(a) (1995) (Connecticut); FLA. STAT. ANN. § 627.4239 (West 1996) (Florida); GA. CODE ANN. § 33-53-2 (Michie 1993 & Supp. 1997) (Georgia); 1992 ILL. LAWS 980 §§ 1-2 (1992, uncodified) (available on LEXIS, 1992 Ill. ALS 980) (Illinois); 5 ILL. COMP. STAT. § 375/6.4 (West 1993 & Supp. 1997) (Illinois); 215 ILL. COMP. STAT. §§ 5/370r, 125/4-6.3 (West 1993 & Supp. 1997) Illinois); IND. CODE ANN. § 27-8-20-7 (Burns 1993 & Supp. 1997) (Indiana); LA. REV. STAT. ANN. § 22:215.18 (West) (Louisiana); MD. CODE ANN., INS., § 15-804 (1997) (Maryland); MASS. GEN. LAWS ANN. ch. 175 §§ 47K-L, 47O-P; ch. 176A §§ 8N, 8Q; ch. 176G § 4G (West Supp. 1996) (Massachusetts); MICH. COMP. LAWS ANN. §§ 500.3406e, 500.3616a (West 1996) (Michigan); N.C. GEN. STAT. §§ 58-67-78, 58-51-59 (Supp. 1996) (North Carolina); N.D. CENT. CODE § 26.1-36-06.1 (1997) (North Dakota); OHIO REV. CODE ANN. § 1751.66 (Banks-Baldwin 1997) (Ohio); OKLA. STAT. ANN. tit. 63 §§ 1-2604, 1-2605 (West 1996) (Oklahoma); R.I. GEN. LAWS §§ 27-55-2, 27-55-3 (1996) (Rhode Island); S.C. CODE ANN. § 38-71-275 (Law. Co-op. 1996) (South Carolina); TENN. CODE ANN. § 56-7-2352 (1997) (Tennessee); UTAH CODE ANN. § 26-18-105(7) (Supp. 1997) (Utah); VA. CODE ANN. § 38.2-3407.5 (Michie 1997) (Virginia).

[5] *Id* at 77, *citing* 59 Fed. Reg. at 59,821. *Accord, e.g.,* 52 Fed. Reg. 8798, 8803 (Mar. 19, 1987) (reaffirming legality of off-label use); 48 Fed. Reg. 26,720, 26,733 (June 9, 1983) (reaffirming legality of off-label use); 40 Fed. Reg. 15,392, 15,393-94 (Apr. 7, 1975) (reaffirming legality of off-label use); 37 Fed. Reg. 16,503, 16,503-04 (Aug. 15, 1972) ("[o]nce [an approved] new drug is in a local pharmacy . . . the physician may, as part of the practice of medicine, lawfully . . . vary the conditions of use from those approved"); FOOD AND DRUG ADMIN., COMPLIANCE PROGRAM GUIDANCE MANUAL No. 7382.900 pt. I, at 7 (1992) ("physicians may use devices for off-label uses (This is considered within the practice of medicine)").

[6] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 214, 111 Stat. at 2348 (codified at 21 U.S.C. § 396 (FDCA § 906)).

as they see fit in the best interests of patients. The Alliance strongly disagrees with the recommendation that FDA seek the statutory authority to consider off-label use when determining intended use. The FDA currently has more than adequate enforcement powers relating to off-label matters. Any additional authority could improperly hamper the practice of medicine, as physicians rely on the ability to use approved devices to treat conditions that are closely related to an indicated condition. It is not uncommon for some uses of medical products to become standard of care in the practice of medicine before there is approval or clearance of the labeled indications for use for a particular product.

"Indications for Use" and "Intended Use". Similarly, the Alliance does not support CDRH's recommendation to combine the terms "indications for use" and "intended use." First, "intended use" is a statutory term, *see e.g.* 21 U.S.C. §360(c)(i)(a)(A), and that statutory language must be honored. The phrase "indications for use" is found in regulations, not statute; and the combination of these terms would improperly blur the distinction between these terms. Moreover, the combination of these terms would require FDA to amend multiple prior regulations and guidance to reflect the new standards and terminology.

Second, combining these terms would impact the practice of medicine and could limit physicians' access to medical technologies that could improve patient care. For example: under current rules, forceps might have a proposed labeling claim saying its intended use was "to grasp and hold objects or tissue" and thus surgeons could apply its use to a wide array of disease states and stay within the general labeling. However, to add "indications for use" for a specific type of tissue or in a particular procedure such as heart surgery to the labeling would perhaps trigger new review cycles or otherwise unnecessarily add to the regulatory burden on the agency and other stakeholders. Combining these terms could allow reviewers to interpret this guidance such that the company would be forced to demonstrate the clinical benefit of a forceps as a bone or heart device, rather than just the more straightforward, yet broad "intended use." This potential for misinterpretation will burden manufacturers and the FDA, but ultimately it will be physicians and patients who suffer if device clearance is delayed or denied due to new regulatory requirements. Forceps are one example of devices that are essential to a surgeon's practice of medicine, whose access could be limited if manufacturers were forced to study and prove all possible indications. Rather, the determination of the appropriate use of the product should rest in the hands and judgment of the experienced physician. The Alliance fears that combining the terms "indications for use" and "intended use" could have significant unintended consequences for the practice of medicine and opposes combining the terms.

Third, the combination of these terms may result in many products being needlessly forced into new premarket approvals which would slow clearance for marketing without benefiting patient safety. As such, the combination of these terms will lead to delays in product reviews and confusion as to when filings are required. Rather than combining these terms, the Alliance encourages FDA to, through Administrative Procedures Act ("APA") rulemaking, explicitly define and distinguish the terms "indications for use" and "intended use" based on current statutory definitions and existing concepts. These definitions should clarify but not change the existing meaning of these terms.

Rescission Authority. The Alliance supports FDA's authority to rescind specific 510(k) clearances obtained by fraud or due to safety concerns when necessary to protect patients. Fundamentally and obviously, fraudulent conduct must not be permitted. However, we do not support an expansion of FDA's rescission authority to 510(k) clearances for reasons other than fraud and safety concerns, as such expanded authority would call into question the legal marketing status of each device that had subsequently relied on the rescinded device as a predicate, even if there is no evidence to suggest subsequent devices are subject to the same inadequacies as the rescinded predicate device. The Alliance believes that subsequent 510(k)s that utilized the rescinded product as a predicate should not be affected unless FDA finds that the subsequent, related devices present a significant public health risk under a section 360(e)-type process or that they also involve fraudulent conduct by the applicant. Stated simply, the rescission of one product ought not, necessarily, to