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

Coalition of Medical Device Manufacturers – Comment (posted 10/14/10)

FDA-2010-N-0348-0057

[redacted]

Comments regarding the Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations

Docket No. FDA-2010-N-0348

I. INTRODUCTION

A. About the Coalition.

The coalition is a group of medical device sector stakeholders that support advancing patient health, encouraging medical device innovation and are committed to a strong, effective FDA. Our efforts are led by the **Medical Device Manufacturers Association** (MDMA), **Medical Imaging and Technology Alliance** (MITA), **California Healthcare Institute** (CHI), and **LifeScience Alley** (LSA). Our broader membership includes multiple stakeholders in the medical device sector, including small and large companies, inventors, investors, regional trade associations and more.

B. Guiding Principles for Reform.

We are committed to balanced, constructive, and well-informed engagement with FDA and other stakeholders to develop responsible reforms and advance patient benefit and medical innovation. The coalition is dedicated to ensuring that improvements made to the FDA's 510(k) review system follow these principles:

- Reforms must promote public health and protect patient safety;
- Reforms must support and enhance continued innovation of, and patient and provider access, to life-saving, life-enhancing medical technologies;
- Reforms to the system should be made after a fair and transparent process;
- Reforms should be based on sound science, data and evidence of need; and,
- Reforms should ensure that product reviews and regulation are conducted in a predictable, transparent, timely, resource-effective, and responsive manner.

II. PROCEDURAL RECOMMENDATIONS

We note that FDA has begun its reform effort admirably by reaching into its organization to solicit employee suggestions and by reaching out through town hall meetings and other mechanisms to seek initial stakeholder comment on its proposals. Under the leadership of Director Jeff Shuren, we anticipate and appreciate continued attention to transparency, stakeholder consultation, and sufficient notice and opportunity for comment. We would highlight several opportunities in this regard:

A. FDA should prioritize proposals and proceed sequentially.

We recommend that the FDA not attempt to implement at one time any significant subset of the proposals set out in the two reports. Rather, the coalition recommends that FDA solicit the public's sense of priorities and focus on those high-priority elements by making subsequent, detailed proposals, and providing additional notice and opportunity for comment. By prioritizing among the 200+ pages of proposals, stakeholders can then provide focused, detailed responses on the most likely agency actions. Such a process would conserve agency resources, reduce the burden on stakeholders, improve the quality and specificity of proposals and responses, and speed the completion of the 510(k) reform effort. Additionally, given the costs of the commissioned IOM 510(k) report, we urge the FDA to wait for those recommendations before evaluating any changes.

In setting the agency's priorities, FDA should consider the direct and societal cost of their proposals, including cost and burden on the agency, patients, manufacturers, and providers; and to consider the impact of delays in clearance, scuttled product development, reduced innovation, and lost jobs. Unwise changes have the very real possibility of increased cost of products, delayed/denied access to products, lost jobs, export of R&D, negative impact on the economy and adverse impact on the trade balance.

We do not believe that it is possible for the agency and industry to implement any significant number of the contemplated changes at the same time without bringing the system to a grinding halt. Prioritization is necessary to avoid such a collapse.

B. FDA should continue and expand transparency.

We recommend that FDA give stakeholders access to the FDA Task Force reports the agency used to prepare the Task Force recommendations. Doing so would enhance public comments, provide greater understanding of the agency's thought processes, issues, priorities, analytical methods and data, and be more in line with FDA and Administration transparency initiatives.

C. FDA should ensure further Notice and Comment on specific proposals.

The coalition and other stakeholders seek to work with the agency to develop improvements to the 510(k) system that strike the right balance of protecting patient safety and fostering innovation in an effective, efficient manner that minimizes unnecessary burden on the agency and industry. To do so, stakeholders need more specific, detailed recommendations on which to respond. Prior to publication of any final guidance,

regulation, or policy change, we urge that FDA go through a second round of notice and comment to receive feedback on specific, detailed proposals. Until finalization of any new guidance or regulations, the FDA ought to avoid "informal" adoption of any proposed changes.

D. FDA should exchange information and perspectives directly with stakeholders.

The coalition encourages FDA to consider engaging directly with stakeholders in real-time, in-person meetings to discuss reform proposals. For example, the coalition conceptually supports improvements in the de novo process. However, the August 4th proposals did not specify how the de novo process was to be improved. Process changes could either make the de novo process effective and efficient or could make it unworkable. Without knowing the specifics, all the coalition can do is to express its philosophical agreement with improving the de novo process. In addition, the de novo process reforms are potentially affected by other reforms in the proposals, notably reforms in the area of predicates. FDA would benefit most from stakeholder involvement that responds to specific proposals and that is delivered in face-to-face exchanges of information and perspectives; and not delivered in response to generalized proposals or delivered in sterile exchanges of written comments over long periods of time.

E. FDA should increase the time allowed for comments.

We recommend that FDA increase the amount of time during which comment on the proposals may be accepted. For the FDA to work through these complicated, interrelated concepts, the agency needed a year of analysis and 200+ pages of discussion. Indeed, the complexity of these issues is illustrated by the fact that it took FDA more than two months longer to issue the initial report than envisioned in the 2010 CDRH strategic plan. Given the complexity of the issues, the multi-dimensional aspects of all of them, and the significance of these proposed changes on patients, providers, industry stakeholders, payors, and investors, not to mention the agency itself, we believe that providing external groups a mere 60 days for comment on FDA's findings is unwise. A longer comment period would allow for more thoughtful input.

Moreover, no crisis exists that demands the FDA to make hasty decisions or take ill-informed action that risk causing unintended adverse effects. Additionally, asking for stakeholder comments on such major issues as creating new classes of devices within such a short time period seems unnecessary, as one would hope any final FDA recommendations be informed by the other bodies analyzing 510(k) reform options, namely the Institute of Medicine and Congress, which are operating on separate, longer timelines. All stakeholders should be concerned about serial changes to similar parts of the 510(k) system.

We urge FDA either to extend the comment period or make other provision for accepting, considering, responding to, and acting on those stakeholder comments.

III. KEY THEMES IN THE COALITION'S VIEW OF THE CDRH PROPOSALS

The coalition has assessed the various proposals found throughout the August 4th documents and combined our comments into common themes or categories. The coalition has not responded to each FDA proposal; on issues where we are silent, such should not be interpreted to indicate the coalition's support or opposition. Likewise, the coalition's support or opposition to broad concepts should not be taken as support or opposition to specific, detailed proposals advanced to implement the broad concepts. The details of implementation can substantially impact the workability of any proposal. We intend this to help provide a better understanding of both the broad areas of agreement and the interrelated nature of many of these proposed changes.

A. FDA must continue to ensure patient safety.

- Protection Against Fraud: The coalition supports FDA's authority to rescind specific 510(k)s obtained via fraud when appropriate to protect patients. Such FDA authority should not impact subsequent 510(k)s that utilize the subject predicate that were not fraudulently obtained, unless FDA finds under a 360(e)-type process that related devices present a significant public health issue.
- Limited Human Testing: Clinical testing on human patients should be limited to those situations where it is essential to provide data in order for the agency to make the relevant regulatory determination. When such clinical information is needed, the agency should look to all sources of clinical data, not just pharmaceutical style blinded, placebo controlled studies or similar types of clinical trials.

  Clinical data requirements should be limited to this small subset of 510(k) products, given the inherent risk that such testing poses to the human subject and the increase in cost, burden and time on both the sponsor and the agency. The agency should specify the limited requirements to submit clinical data.

  The coalition supports use of bench and non-clinical testing, and innovative and high-tech alternatives to experimental clinical testing on patients whenever possible and appropriate, and FDA should explicitly permit the use of clinical information from actual practice, literature, or other regulatory submissions.

  Research to date establishes that more human clinical testing does not increase product safety. Indeed, analysis of recent CDRH Class I recall data presented to IOM[1] indicate that 55% of recalls relate to post-market issues and thus are not prevented by additional human clinical trials. Of the recalls due to premarket issues, 75-80% of these are due to design issues, which illustrates the importance of improved QSR (design controls, etc) and not necessarily human clinical trials. Bench testing and design controls should be used to identify design issues without endangering patients or increasing the burden on the sponsor and the agency. Of

[1] R. Hall: Using Recall Data to Assess the 510(k) Process, IOM Public Meeting, July 28, 2010. http://www.iom.edu/~/media/Files/Activity%20Files/PublicHealth/510kProcess/2010-JUL-28/06%20Hall.pdf

the recall data analyzed, there were no recalls identified relating to newly discovered clinical risks, and only 7% of recalls were for inadequate labeling issues (potential surrogate description of newly discovered risks, but which also could include human factor issues). These data show that additional human clinical studies would have very little impact on Class I safety recalls. A second study presented to IOM also supports the above conclusions.[2]

- Expanded use of abbreviated and special 510(k)s: The coalition supports expanding the use of abbreviated and special 510(k)s in order to permit faster patient access and the allocation of FDA resources to more substantive submissions. Everyone benefits if resources are focused on the substantive questions. The coalition supports the current standard for when to submit a device modification for clearance.
- Unique Device Identification: The coalition supports the use of Unique Device Identification (UDI) for existing post market requirements. Tracking devices throughout the life of the product using UDI will enhance patient safety. However, industry input on the mechanics of implementation is needed before any such policy goes into effect.
- Off-Label Use: The coalition opposes any statutory changes involving off-label use. FDA currently has more than adequate enforcement powers relating to off-label matters. More significantly, this concept could limit the ability of physicians to act in the best interest of patients. As such, it is contrary to express statutory requirements that the agency not regulate the practice of medicine. It could also require companies to submit unnecessary information to FDA having nothing to do with the company's activities or objectives.

B. FDA should substantially maintain the current scope of the 510(k) system.

- Collective Effect of CDRH Proposals: The current set of proposals will, to the extent details are available and predictions can be made, in totality reduce substantially the number of products that will be eligible for review under the 510(k) system. Any change to the overall scope of the 510(k) must be made through statutory changes and not indirectly through a combination of multiple changes to varying parts of the process. While the agency's individual proposals will be discussed separately, FDA should consider and publically address the overall scope issue. FDA should make public the anticipated effect, if any, on the number of products eligible for 510(k) consideration for each proposal and for the total effect of all the proposals. This is necessary for stakeholders and policy makers to understand the overall effect of any change.

[2] W. Maisel: Premarket Notification: Analysis of FDA Recall Data, IOM Public Meeting, July 28, 2010. http://www.iom.edu/~/media/Files/Activity%20Files/PublicHealth/510kProcess/2010-JUL-28/05%20Maisel.pdf

It is also necessary for the agency to have a good understanding of the impact that substantial changes in scope may have on its own resource burdens; its ability to review products in a timely, predictable, and transparent way; and to understand the impact on stakeholders. The agency should be extremely cautious about making any dramatic shifts in scope for these practical reasons alone.

The coalition generally supports the notion that certain reforms are needed to improve the 510(k) system; however, the system should not be altered in such a way as to measurably reduce the number of products eligible for 510(k) clearance as such would limit patient access to life-saving, life-enhancing medical technologies and hamper innovation. (Similarly, the proposals should not substantially increase the number of products or product changes subject to 510(k) clearance, for example, by changing the exemption status of products or requiring submissions for modification to 510(k) products that do not current require a submission.) The coalition recognizes that a few specific product types might be up-classified or down-classified due to new information but we believe the overall scope of the program should remain as is.

- "Intended Use" and "Indications for Use:" FDA should not combine "intended use" and "indications for use." These terms reflect substantive differences and serve different purposes. "Intended use" is a statutory term (see, for example, 21 USC §360c(i)(1)(A)) and that statutory approach must be honored by all. Combining these terms will blur regulatory lines and force many products into new PMAs with no corresponding patient benefit. Combining these terms will lead to confusion over when filings are needed and cause delays in product reviews.

  Furthermore, the combination of these terms would require FDA to amend multiple prior regulations and guidance to reflect the new standards and terminology.

  The coalition recommends FDA explicitly define and distinguish (through rulemaking) the terms "intended use" and "indications for use" based on current statutory definitions and existing concepts. Any improved definitions should add clarity but not change or alter the existing definitions of these terms. FDA and all stakeholders should adhere to these definitions in all written material and decisions. The coalition believes all stakeholders could benefit from clearer guidance within existing statutory and regulatory bounds on the characteristics of "intended use" and "indication for use."
- Split Predicates: The coalition does not support the elimination, or significant limitations on, the use of split predicates. Split predicates are a valuable way to provide robust product reviews as information from different areas is brought to bear in the submission examination. The need for, and use of, split predicates reflects the nature of current health care practice. Combining already proven technologies permits better patient care and more efficient delivery of health care. Restricting the use of split predicates will hamper innovation and increase costs. Moreover, there is no statutory or regulatory basis to prohibit or limit split predicates.
- Multiple Predicates: The use of multiple predicates should not be restricted. Current practice (with improvements for administrative efficiency, predictability and certainty) properly permits the use of multiple predicates. Narrowing the scope of multiple

predicates hinders innovation, and products that utilize multiple predicates often provide improved patient care more efficiently. As the 510(k) system moves forward, more and more 510(k) cleared devices will exist that can serve as predicates. FDA should not encourage limiting the number of predicates brought to FDA's attention.

Along the same line, the coalition supports appropriate bundling of sufficiently similar products. Thus increases efficiency for both the agency and industry. It also permits more consistent product review. The coalition understands that bundling should not be permitted with dissimilar products.

- Functional Indications: FDA should consider increased utilization of functional indications as such indications are consistent with current medical practice and provide physicians with needed information and products which improve patient care. The use of functional indications is successful in other jurisdictions and supports the statutory prohibition on FDA becoming involved in the practice of medicine. Similarly, FDA should not limit the use of general indications or impose additional requirements on specific indications.
- 510(k) Flow-Chart: The coalition supports clarity in all guidance, including the 510(k) flow chart. The coalition encourages FDA to revise and update the 510(k) decision tree to give stakeholders more clarity on when 510(k) applications are appropriate, and when new applications are needed as a result of changes to products or indications. Efforts to clarify the flow chart should not be a disguised effort to limit the scope of the 510(k) system or to push any meaningful number of products from the 510(k) system into the PMA system. FDA should ensure that minor changes in products or uses do not trigger unnecessary submissions, as any such submission requirement ultimately means delays in getting the product to the patient. The coalition recommends FDA consider updating the flow-chart concept by beginning with four separate elements to be considered (predicate indications and intended use, technology, data requested) and then provide clear references to the data requirements and relevant guidance associated with each element. The coalition recommends FDA consider updating the flow-chart concept by beginning with four separate boxes (predicate, indications and intended use, technology, data request with references to the data requirements and relevant guidance associated with each element.

C. FDA should use product-specific controls, not create a new Class IIb.

- Authority and Rationale: Although there is some ambiguity in the FDA proposals over how FDA will approach possible Class IIb products, the coalition does not support the creation of a new Class IIb. First, FDA lacks the statutory authority to create a new class. Assuming the agency wants to create a Class IIb as a heuristic mechanism to solve some undefined problem, even this approach is flawed because, regardless of how the change is framed, the result would be the adoption of a new, broad set of requirements that apply across multiple different products, and that is the definition of a class. New classes require statutory authority, and the FDA obviously cannot avoid

this requirement by framing Class IIb as something less while accomplishing the same result. FDA cannot use guidance to create this new Class IIb.

Furthermore, the FDA has not shown that there is a group of 510(k) products that, as a class, require some additional requirements. FDA should set forth the data supporting the need for such a new classification before requesting public input on a specific proposal.

- Product-Specific Basis: The FDA should consider any new Class IIb-like requirements only after product-by-product consideration, as required by the statute, and as the most effective way to match requirements to products and therefore to effectively improve patient safety. Broad, automatic requirements based on classification rather than specific risk profiles and product characteristics would not effectively benefit patients, would disrupt innovation, and would delay patient access to products.

  The coalition understands that the agency may, on a case-by-case basis, have reason to demand specific, additional requirements for select products. The recent infusion pump initiative is an example of such a focused, directed activity. But class-wide special controls, as described by CDRH, are not an appropriate use of special controls. These should be – and are required to be – product-specific. The various specific requirements being considered for Class IIb are not value added. For example, there is no showing that requiring Class IIb-wide clinical data would be value added for many products that might be considered for inclusion in Class IIb. Likewise, there is no showing of any need to increase the number of submissions for which clinical data should be submitted. Analysis of 510(k) data establishes that the significant majority of post-clearance safety issues do not involve the absence of premarket clinical data. QSR systems are a better approach to improving product performance rather than requiring submission of non-value added clinical data.

- Consequences: We note that there is a substantial concern that there will be tendency to "up classify" devices into Class IIb and to place products going through the de novo process automatically into Class IIb. This tendency or approach must be avoided. Products must be individually assessed and assigned to product classifications based on established risk management principles.

- Workability: We note that tiering within existing classes historically has failed: FDA tried a form of tiering within classes in the 1990s when it assigned a tier 1, 2, or 3 designation to products within the various statutory classes. The tiers were intended, among other functions to help set priorities and analytical needs. By most accounts, and as reflected in the ending of this process in the late 1990s, the additional tiering efforts (and, creating a Class IIb is simply tiering within Class II) consumed unjustifiable time and effort, failed to keep up with innovation and changes in products, and resulted in difficult to sustain distinctions. Before proceeding further with the Class IIb concept, FDA should publicly discuss the 1990s effort at tiering and explain why this new Class IIb is somehow different and more workable.

D. FDA should ensure predictable, timely, efficient, and quality review process.

- Administrative Processes: The coalition supports improving the administrative processes used by FDA. The coalition agrees that improved databases that include more non-proprietary information would be beneficial for all stakeholders. This could include linkages between predicate devices and improved product codes. Certain information, such as 510(k) summaries, should be prepared with industry input to ensure accuracy and the protection of confidential information. Standardized electronic templates could also be useful. These administrative improvements, however, cannot be permitted to increase review times, decrease certainty or add burden without specific, demonstrated patient benefit exceeding this harm.
- Labeling: The coalition supports submission of final labeling provided that there is no "labeling review" that delays clearance or marketing. Likewise, CDRH already has access to all label modifications through inspections or subsequent submissions so CDRH should not require those not triggering a 510(k) submission requirement to be submitted to the agency. Requiring all minor label changes to be submitted adds nothing to patient safety and simply increases the burden on CDRH and industry.
- De Novo Process: The coalition supports a more effective, efficient, timely and predictable de novo process. To improve the de novo process, the coalition recommends FDA consider: 1) eliminating the need to go through the 510(k) (NSE) process prior to commencing the de novo process, 2) ensuring that classification decisions are based on legitimate risk assessments and the need to ensure patient access to new products, 3) creating defined time periods for key process steps, 4) creating a fast track de novo process for obvious Class II products and 5) eliminating the need to create new regulations or special controls unless needed on a case-by-case basis. FDA should ensure that data requirements are logical and relevant, and that the changes improve timeliness and predictability of review.

  The coalition recommends that FDA better define the de novo process and clarify the types of products and circumstances that can be handled under the de novo process. This should include specific time frames for each step in the process with FDA making public its performance compared to these time requirements. The coalition also suggests FDA consider use of a very general, no-guidance special control (e.g. for “clinical information” or "clinical data") and then later requiring a synopsis of the information actually used for the prior clearances. The coalition urges the FDA to ensure that changes do not result in an influx of submissions being subject to de novo as a result of reviewers finding that products are not exactly the same as the suggested predicate or, in conjunction with other Task Force proposals, result in de novo products being equated to PMA or a PMA-like pathway.
- Third Party Review System: The coalition supports the third party review system. It has proven to be an effective, efficient system to get low-risk products to patients faster and without burdening CDRH. The coalition urges FDA to establish clear guidance for when and how third party review is appropriate, to define the process for

reviewing third party recommendations in order to avoid duplicative reviews, to extend the scope of products that are eligible for such reviews, and to establish performance goals to promote better visibility FDA's performance and review times.

FDA should ensure that any changes do not result in more than a de minimis decrease in the number of products eligible for third party review and that FDA not put in place other obstacles to using third party review. The coalition is concerned with the existing perception that the agency will simply ask for clinical data in order to pull a product from third party review. Hopefully this perception is inaccurate but there should be clear guidance as to what products are eligible for third party review regardless of whether clinical information is submitted.

Likewise, the coalition supports increased training for CDRH and third party reviewers and increased access to information on other clearances (subject to protection of confidential information and appropriate handling of conflicts of interest).

- Ad hoc review teams: Additionally, the coalition supports the creation of ad hoc teams of experienced reviewers to provide temporary assistance to address backlogs and surges.
- Notices and Guidances: The coalition supports enhanced communication from CDRH to industry. However, CDRH should ensure that there is adequate public input before final guidance is promulgated. Excessive or improper use of "immediately effective" guidances or "notices to industry" raise administrative law issues and conflicts with good guidance practice requirements. The coalition supports transparency and public input and is very concerned that the "notice to industry" will bypass this important (and required) step. Transparency requires public disclosure of the proposed policy change and opportunity for public input to precede formal or informal implementation Going directly to “immediately effective” guidance or using "notices to industry" runs afoul to administrative law rules and transparency principles.

  The coalition believes guidance documents should to be prepared more quickly and draft guidances should not be allowed to remain in that status for long time periods.

  The coalition supports the drafting of proposed guidance by various stakeholders. For proposals which are particularly complex or will have a significant impact on patients, provides and the industry, there would be value in stakeholders having the ability to exchange information and perspectives on specific proposals face-to-face and not just through sterile, written exchanges of documents.
- Limitation on Use of Prior Predicates: Current FDA authority provides the agency with the ability to ensure that an unsafe product will not be marketed, regardless of existing predicates. As such, it is unclear whether there is a real need for a process to limit the use of a particular predicate. The coalition is not aware of any meaningful number of products cleared based on "bad" predicates.

  We specifically note that FDA currently has the statutory authority under 21 USC §360c(i)(2) to prevent a "bad" predicate from being the basis for a future clearance. Various procedural protections are built into the current system and will be needed if any new approach or process is adopted.

In any event, if such additional authority is sought, it may require statutory changes or at least new regulations; guidance alone is not sufficient to affect such important third party rights without rulemaking. Any such restriction on the use of an existing predicate must go through a public process at least similar to the existing 360e process.

- "Least Burdensome" Provisions: The coalition supports the statutory "least burdensome" requirement and earlier efforts to implement least burdensome in an effective manner throughout CDRH. CDRH should apply this requirement within the letter and spirit intended by Congress in 1997. It is inappropriate to translate "least burdensome" as "reasonably burdensome." Any guidance revision should ensure that least burdensome is applied and interpreted pursuant to the Congressional mandate.
- Quality of Submissions and the Use of Assurance Cases: The coalition supports high quality submissions and notes that CDRH has the authority to reject below-standard submissions. The coalition does not support the mandatory and widespread use of an assurance case methodology. Assurance cases are simply one method among many to assess product designs or predicate comparisons, and FDA has not demonstrated how assurance cases specifically will improve patient safety. FDA should not focus on any one method. Rather, CDRH and industry should use ISO 14971, other design validation systems and QSR concepts and provisions to select and implement the most appropriate method for the particular product, rather than follow a mandated, one-size-fits-all approach.
- Responding to New Science: The coalition supports the creation of a transparent Center Science Council and is interested is CDRH's views on improving processes for responding to new science. The coalition believes any process for responding to new science should include industry involvement with the identification and assessment of new scientific matters.

  The coalition awaits more detail on the responsibilities and processes of the new Center Science Council. It is unclear, for example, how the role of the Center Science Council will impact the current internal and external dispute resolution processes and the role of the ombudsman. The coalition does not support giving the Center Science Council authority to reverse decisions.

  In both the creation and the functioning of the Center Science Council, FDA must proceed carefully to ensure that all administrative law requirements are satisfied, and CDRH should make public, with an opportunity for stakeholder input, its initial proposals for this council's role, responsibility 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. All stakeholders should have input into the processes, role, and responsibility of the new council.
- General Need for More Training: The coalition supports additional training at the various levels of the agency. A number of recommendations throughout the 200 pages of material point out the need for training. The survey of reviewers and management also confirms the need for training. If FDA staff does not understand the rules, then FDA is hard pressed to criticize industry for misunderstandings or mistakes.

- Science and Technology Training: The coalition supports additional training on relevant scientific and technical areas but urges FDA to focus training on those aspects that are relevant to FDA's statutory mission, processes and objectives. Too many times, someone at FDA has asked a question for personal curiosity rather than because the information is relevant to the review process. Training should seek to curb this problem and should be focused on what the individual needs to fulfill his or her statutory obligations.

  Industry and other stakeholders should be value added participants in such training. Reviewers should be encouraged to visit manufacturing facilities, research and engineering campuses, and relevant sites in the field, and learn firsthand about new technology, science, and technical matters. The coalition encourages FDA to consider a public-private training partnership to facilitate ongoing agency familiarity with the latest management techniques. FDA should also utilize academic, government and industry expertise to advise FDA on emerging scientific developments.
- Legal and Regulatory Training: As part of FDA's efforts to improve the 510(k) system , the coalition supports adequate training for FDA reviewers. Such training must include training on the legal requirements that bind both industry and FDA. Training must include rigorous instruction on legal and regulatory rules, processes and systems. As the internal survey demonstrated, too often FDA itself does not know the legal requirements. This leads to inappropriate questions and requests for information, incorrect and inconsistent decisions and uncertainty and delay. First and foremost, FDA is a legal regulatory and enforcement agency. FDA staff must understand those rules above all else.
- Standards Training: The coalition supports the use of consensus standards and supports training of reviewers on how to use such standards to avoid unnecessary work by either FDA or industry.

E. FDA should ensure that additional data requirements are justified by benefit to patients relative to burden.

- Use of Relevant Data: The coalition supports the use of data to improve the 510(k) process and ensure patient safety, including the submission of relevant, material and non-duplicative scientific information in appropriate situations. However, CDRH should not require excessive, duplicative, or non-value added submissions. There may well be thousands of articles relating to established and long-marketed products. CDRH should ensure that the relevant scientific information is provided to FDA without regard to source or format. Requiring "all" literature, for example, would unnecessarily burden FDA and industry for no added value. The coalition supports high quality clinical data in appropriate situations, but notes that "high quality clinical data" does not and should not necessarily mean clinical trials. CDRH should not require clinical data for the significant majority of 510(k) submissions. Review and assessment of clinical data issues and IDE challenges should include industry participation.

Furthermore, the agency currently has the statutory authority to require the submission of "information respecting safety and effectiveness" of the device at issue. See 21 USC §360c(i)(3)(A) and (B). It is unclear whether the agency requires any additional authority.

- Predicates as a Data Trigger: The simple fact of the number of predicates used should not trigger additional scrutiny. As time goes on, product submissions will have more and more predicates. In addition, FDA should not discourage companies listing multiple predicates as those listings can enhance FDA's review of the specific submission.
- Manufacturing Information: CDRH has generally no need nor the expertise for detailed manufacturing information. Other than increasing the burden on FDA and industry, there is no evidence to support the notion that agency review of manufacturing information would enhance product safety. As discussed below, even if CDRH creates a narrower group of Class IIb products, requiring manufacturing information will result in nothing more than increased review time, causing unnecessary delays in getting products to patients, and result in additional burden and costs on the agency and all other stakeholders.
- Physical Specimens: There is little agency benefit but much industry burden in forcing industry to maintain a physical specimen of all 510(k) products. For example, how would the agency appropriately handle highly expensive capital equipment or products with multiple iterations such as size differences? For products like imaging machines which are often very large (some are room sized) or certain products which must be stored in climate-controlled, stable environments, the physical specimen requirement would be incredibly burdensome in the short term, and unworkable in the long term. It is hard to imagine a situation in which the existence of a physical specimen would be of value to FDA years after product clearance. Stated differently, the existence of such specimens does not link to any statutory role of FDA.
- Device Modifications: The coalition does not support a requirement that all modifications, no matter how minor, be submitted to CDRH in some filing made every 3 years or so. First, there is long standing guidance that describes when a submission is needed for some change. That guidance properly separates significant modifications requiring a new clearance from minor modifications which do not. We also note the current regulatory system establishes that modifications should be submitted in cases in which the change could significantly affect safety or effectiveness. That standard should be maintained.

  Second, just because a company may not have applied that test correctly in the past is not the reason to force industry and the agency to deal with a flood of information.

  Third, FDA currently can learn about such changes in inspections and in subsequent submissions. A requirement that all modifications be submitted, even as part of an annual (or less frequent) report would burden FDA with meaningless changes and increase the burden on industry for no benefit. (We also note that the change would already have been made without FDA oversight and so this seems like closing the barn

door after the horse has left.) Furthermore, if the company did not make a submission as required, the agency can consider enforcement action.

Fourth, the agency's expressed concern is that companies are implementing modifications without necessary clearances, but if a company is going to break the law (deliberately or inadvertently), requiring some filing 2-3 years later wouldn't make a difference.

Finally, by the time the report goes to the agency, the feared change will have already been made and be on the market for a substantial time. Any such requirement along the lines suggested simply doesn't address the issue raised by the agency.

Perhaps the answer lies elsewhere. QSR systems are in place to ensure that changes are assessed and validated. Likewise, including literally all modifications in a submission adds burden for no benefit. At the very least, any such new obligation must include a de minimis level. The coalition believes submissions should include only relevant or material changes from the predicate device; there is no reason to require anything more.

- "Conditions of Clearance:" CDRH currently has more than adequate post market requirements including special controls (see 21 USC §360c(a)(1)(B) and 522 orders. The agency neither has the need nor the authority to create "conditions of clearance." Given the predicate-based 510(k) system, such an approach would not add any value and would not link products and clearances with relevant post market data. Despite the futility, even if FDA wanted to adopt a "conditions of clearance" approach such a change would require statutory authority.

F. FDA should ensure reasonable public access and transparency in the 510(k) system.

- Public Metrics: The coalition strongly supports the creation of relevant public metrics relating to the performance of the 510(k) system. These metrics should include measures of whether various submission requirements enhance patient safety and benefit as well as time periods (by division, branch or other subset) for actual FDA review time and for total cycle time including industry time. To the extent that gaps are noted in performance or value, CDRH should take steps to address the issues. This must also include specific periodic review of regulatory requirements that should be eliminated if they are determined not to be relevant to patient safety and effectiveness. The coalition recommends the joint development of metrics to ensure regular and timely communication between the agency and stakeholders.
- Transparency of Applicant Information: The coalition supports clarity in submissions including placing information currently required in a 510(k) submission into a single section. Likewise, high level schematics or photos may have a place in submissions if they aid in review. These should be for internal, FDA-use only and not be made public, as such could implicate trade secrets.
- Transfers of ownership: The coalition sees value in disclosing to FDA transfers of ownership from one company to another and eventual posting on FDA's website.

This requirement must be timed so as not to prematurely disclose highly confidential corporate transactions such as acquisitions.

- Transparency of FDA Information: The coalition supports bi-directional disclosure of information given to and provided from the agency. We urge the FDA to improve transparency and efficiency throughout the review process by using information technology to, e.g. track review status and report on outcomes; improve the content of and search capabilities in the 510(k) database, the product code database, the recall database, and the guidance document database; incorporate standardized data elements in databases beyond current high-level categories in order to improve functionality and accuracy of these data bases. The coalition also recommends FDA publicly discloses all new or modified requirements (data or other requirements) to enhance stakeholders' knowledge and certainty of data requirements. Additionally, the coalition supports public audits of the 510(k) system, and recommends that industry input be part of any audit. Patients, providers, patients, providers, industry stakeholders, payors, investors, and the agency all benefit from increased transparency of FDA information.
- Accessing Experts: The coalition is interested in how CDRH would address confidentiality, conflict of interest and FACA issues inherent in using social media to access various experts. Additional information on this proposal is needed before the coalition is in a position to fully assess the proposal and offer informed views.

IV. CONCLUSION

The coalition supports a strong 510(k) system that advances public health, patient access to innovation products and predicable, transparent processes. FDA must ensure that the 510(k) reform process itself is done in a deliberative, thoughtful, way that includes assessment of public health, innovation and predictability. As the 510(k) reform process moves forward, the agency needs to provide adequate time for input and additional notice and comment opportunities for each specific proposal. CDRH should consider engaging directly with stakeholders in real-time, in-person meetings to discuss reform proposals. Throughout the process, CDRH must follow its current statutory authorities and ensure compliance with administrative law rules. Any requirement (old or new) should not be maintained unless it materially advances the statutory purpose of CDRH. We urge the FDA to explicitly consider, debate and balance FDA's twin purposes of protecting patients and fostering innovation at every turn.

Respectfully submitted,

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National Association of Manufacturers and U.S. Chamber of Commerce – Comment (posted 10/14/10)

FDA-2010-N-0348-0058

Joe Trauger

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Human Resource Policy
National Association of Manufacturers

Randel K. Johnson

Senior Vice President
Labor, Immigration, & Employee Benefits
U.S. Chamber of Commerce

October 4, 2010

The Honorable Dr. Margaret Hamburg
Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

RE: 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 Dr. Hamburg:

The National Association of Manufacturers and the U.S. Chamber of Commerce, appreciates the opportunity to comment on the preliminary report and recommendations of both the Center for Devices and Radiological Health 510(k) Working Group and the Task Force on the Utilization of Science in Regulatory Decision Making. Signatories to this letter, trade associations representing the interests of businesses, small and large, from all sectors of the economy employing tens of millions of Americans, as well as the medical device industry, strongly believe that an appropriate balance should be struck between government regulation and free enterprise. We are committed to working with the FDA to ensure that private industry is not adversely affected by the recommendations issued in these reports.

Our organizations are deeply committed to policies that will support a vibrant and successful manufacturing sector—a critical ingredient in U.S. economic growth and standards of living. The medical technology industry, comprising manufacturers of medical devices and diagnostics, is a sector of manufacturing where the U.S. leads the world. This industry represents the eleventh largest manufacturing sector in terms of exports, and is one of the few manufacturing sectors that has consistently maintained a favorable balance of trade. The sector, like other manufacturing industries, provides jobs that substantially exceed U.S. average wages and is an engine for jobs in supporting manufacturing and service industries. The prosperity that the medical technology industry brings to many American workers is dependent on an FDA review process that assures efficient and consistent reviews, while protecting patients against unsafe or ineffective products.

Current trends in FDA review of 510(k) products show a troubling pattern of inefficiency and larger burdens on manufacturers that threaten American manufacturing leadership in this vital sector. Whether the issue is total review times, the number of review cycles, the amount of time manufacturers spend answering FDA questions after products are submitted for review, or the withdrawal of applications before a final decision, FDA statistics show performance has declined

substantially since 2003, despite the significant additional resources that the FDA has received from expanded user fees and appropriations.[1]

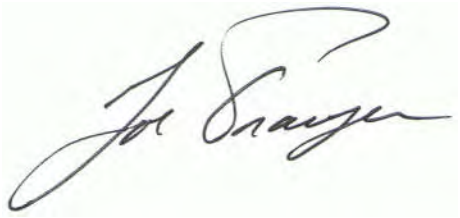
At the same time, the current 510(k) process has an exemplary safety record that does not demonstrate a case for sweeping reforms that would add to manufacturers' burdens in developing products and securing FDA approval. Recent studies by the Battelle Memorial Institute,[2] Professor Ralph Hall of the University of Minnesota[3], and Dr. William Maisel of the Medical Device Safety Institute at the Beth Israel Deaconess Hospital in Boston[4] have all demonstrated that only a very small proportion of approved 510(k) products subsequently show safety problems.

With this backdrop, the National Association of Manufacturers and the U.S. Chamber of Commerce are concerned that many of the proposals developed by the 510(k) working group undermine U.S. manufacturing employment, growth, and competitiveness while not significantly increasing the protection of public health. Our organizations urge the FDA to reject proposals, such as imposing arbitrary limits on acceptable predicates, redefining the term substantial equivalence, and eliminating the separate classification of intended use and indications for use, that alter basic aspects of the current program. These proposals will increase development time as well as costs for manufacturers substantially without a demonstrated need for these additional burdens. Additionally, these proposals could worsen public health by depriving patients of timely access to new treatments and cures. Changes that will increase approval difficulty or time should only be proposed for product types where there is a demonstrated need for additional requirements.

At the same time, we urge FDA to implement proposals on a priority basis that will address the current problems with the review process, including better training of reviewers and managers, and the issuance of more guidance documents.

Finally, FDA should consider the capacity of an already stressed system to absorb additional changes. With more than 50 changes proposed by the task force, any attempt to implement a large proportion of them rapidly would create confusion and necessitate retraining of reviewers and manufacturers that could be extremely destructive to the review process for many years.

Sincerely,



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Vice President
Human Resource Policy
National Association of Manufacturers

Randel K. Johnson
Senior Vice President
Labor, Immigration, & Employee Benefits
U.S. Chamber of Commerce

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[1] FDA statistics: FDA 510(k) Working Group, *Preliminary Report and Recommendations*, Center for Devices and Radiological Health, U.S. Food and Drug Administration, August, 2010.

[2] Battelle: Battelle Memorial Institute, "510(k) PreMarket Notification Evaluation," September, 2010.

[3] Hall, Ralph F. Hall, "Using Recall Date to Assess the 510(k) process," University of Minnesota, Institute of Medicine 510(k) workshop, July 28, 2010.

[4] Maisel: William H. Maisel, M.D., "Premarket Notification: Analysis of FDA Recall Data," Institute of Medicine 510(k) workshop, July 28, 2010.

Advanced Medical Technology Association (AdvaMed) – Comment (posted 10/14/10)

FDA-2010-N-0348-0059

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AdvaMed
Advanced Medical Technology Association

October 4, 2010

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 Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations; Availability; Request for Comments

Dear Sir/Madam:

The Advanced Medical Technology Association (□AdvaMed□) is pleased to provide the enclosed comments and recommendations on the Center for Devices and Radiological Health *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.*

AdvaMed represents manufacturers of medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments. Our members produce nearly 60 percent of the health care technology purchased annually in the United States. These members range from the smallest to the largest medical technology innovators and companies. Nearly 70 percent of our members have less than □30 million in sales annually.

AdvaMed appreciates the opportunity to comment.

Sincerely,

Janet Trunzo
Executive Vice President
Technology and Regulatory Affairs

Attachments

AdvaMed
Advanced Medical Technology Association

Comments and Recommendations on
Center for Devices and Radiological Health
510(K) Working Group Preliminary Report and Recommendations
Task Force On The Utilization of Science in Regulatory Decision Making
Docket No. FDA-2010-N-0348

Submitted by:
Advanced Medical Technology Association (AdvaMed)

October 4, 2010

AdvaMed
Advanced Medical Technology Association

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ATTACHMENTS

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General Comments

AdvaMed commends the 510(k) Working Group (the Working Group) and the Task Force on the Utilization of Science in Regulatory Decision Making (the Task Force) on their thorough review and evaluation of the 510(k) program and the use of science. AdvaMed supports the Working Group's stated goals of the 510(k) program to "(1) assure, through a quality review process, that marketed devices, subject to general and applicable special controls, provide a reasonable assurance of safety and effectiveness; "and (2) "fostering innovation in the medical device industry" and the Task Force's stated goal of making recommendations to CDRH "on how the Center can quickly incorporate new science "including evolving information, novel technologies, and new scientific methods "into its decision making, while also maintaining as much predictability as practical."

AdvaMed also supports many of the concepts outlined in the proposals or elements of the proposals (contingent upon their appropriate implementation under existing statutory authority) contained in the two reports (see our more detailed specific comments below) that we believe will enhance and improve program predictability. These include among others: improving the training and education of reviewers; streamlining the implementation of the *de novo* classification process; establishing collaborative relationships to better leverage external scientific expertise; establishing a Center Science Council to provide oversight and consistency across reviews; posting of reviewer decision summaries and a webpage for new information; a standard template for 510(k) summaries; and documentation of 510(k) ownership transfer.

Nonetheless, we are concerned that the cumulative effect of the multiple CDRH proposals in the two reports would result in a revolutionary change in both the 510(k) process and in the larger regulatory framework and may adversely affect the ability of CDRH to effectively carry out mission-critical functions, including timely reviews. Wholesale changes to the program will also impact industry's ability to efficiently bring new devices to market.

AdvaMed believes proposed changes to the program must also be considered within two important parameters. First, the program as a whole has an admirable safety record. Recent, independent studies by Dr. William Maisel of the Medical Device Safety Institute at the Beth Israel Deaconess Medical Center, Professor Ralph Hall of the University of Minnesota, and Battelle Memorial Institute all show an extremely low rate of recall of medical devices and diagnostics because of safety problems. The Battelle Memorial Institute report is provided in Attachment A.

Second, as documented in the body of the report, there has been a significant deterioration in the efficiency and consistency of the 510(k) review process. If these trends are not reversed, there will be a long-term negative impact on patient access to new and improved treatments and to investment by and in device companies and others in the development of new products. Key statistics demonstrating these points include:[1]

[1] Statistics derived from ODE Annual Performance Reports and FDA's 510(k) report (page 39).

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- The average total 510(k) decision time has risen 20 percent (97 days in 2002 vs. 116 days in 2008)
- The number of days 510(k) submitters spend answering FDA requests for more data has nearly tripled (19 days in 2002 vs. 51 days in 2008)
- The number of review cycles (the number of times FDA "stops the clock" on its review because it has decided to ask the manufacturer for more information) per 510(k) application increased by one-third between 2002 and 2008 (1.4 per application in 2002 vs. 1.9 in 2008)
- The percentage of 510(k)s withdrawn by sponsors has skyrocketed 89 percent from 2004 to 2009 (nine percent to 17 percent).

Importantly, the 510(k) report establishes that review staff fails to consistently interpret regulatory requirements. This suggests that there may be two over-arching root causes leading to inconsistent interpretations: (1) review staff may not be effectively trained; and (2) the guidances they follow are not sufficiently clear. Changes to the existing system will not constitute an improvement unless these root causes are first addressed. CDRH should consider whether improved training, clearer guidances, and guidance development would eliminate the need for some of the proposed changes to the program.

We also urge CDRH to establish clear program metrics. Although the 510(k) and science program reviews were thorough, without established program metrics, some of the proposed changes may be intended to correct problems based on a few outliers or anecdotes when resources could be better targeted elsewhere.

Once the impact of improved training and improved guidance has been assessed, and clear program metrics have been established, AdvaMed recommends that CDRH prioritize and implement a limited number of selected recommendations on which there is general agreement. Once these have been implemented, additional recommendations on which there is agreement can be launched and implemented. A process that tries to implement too many changes at once would overwhelm CDRH, its reviewers and industry, and likely will not lead to improvement. AdvaMed has specific recommendations for those proposals that should be implemented on a priority basis:

- Establishment of a Center Science Council to ensure consistency and predictability in conjunction with metrics to assess whether the new process is effective.
- Revision of the existing guidance to streamline the implementation of the *de novo* classification process and to clarify evidentiary expectations for *de novo* requests.

The table below also outlines at-a-glance the AdvaMed position on each of the 510(k) Working Group and Utilization of Science in Regulatory Decision-making recommendations and sub-proposals within the recommendations. In each case, we have stated whether AdvaMed "supports," "supports with modifications," or "does not support" the recommendation and the basis for our position. Below, please find our specific comments on each of the CDRH recommendations.

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SUMMARY OF ADVAMED POSITIONS ON WORKING GROUP/TASK FORCE RECOMMENDATIONS

CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
510(k) Report			
The 510(k) Working Group recommends that CDRH 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. Several public comments expressed concern that, if these two terms were combined, any proposed change in a device's label indications could be considered a change in "intended use." The Working Group recognizes the importance of providing submitters with the flexibility to propose certain changes to their labeling, without such a change necessarily constituting a new "intended use." Therefore it recommends that CDRH carefully consider what characteristics should be included under the term "intended use," so that modifications that are currently considered to be only changes in "indications for use" and that CDRH determines do not constitute a new "intended use," are not in the future necessarily construed as changes in "intended use" merely because of a change in semantics. Any change in terminology would be intended to provide greater clarity and simplicity, not necessarily to make the concept of "intended use" more restrictive.		✓ Revise existing guidance to *clarify* each term, *not consolidate* terms.	✓
The Center should also carefully consider what it should call the existing "Indications for Use" statement in device labeling and the "Indications for Use" form currently required for all 510(k)s, in order to avoid confusion in terminology but still maintain an appropriate level of flexibility for submitters.		✓ Include indications for use in *labeling* but not *label.*	
The 510(k) Working Group recommends that CDRH develop or revise existing guidance to clearly identify the characteristics that should be included in the concept of "intended use."		✓ Revise existing guidance to *clarify* each term, *not consolidate* terms.	
The 510(k) Working Group further recommends that CDRH provide training for reviewers and managers on how to determine "intended use." Such training should clarify the elements of a device application that should be considered when determining the "intended use," e.g., product labeling, device design (explicit or implied), literature, and existing preclinical or clinical data. Training on "intended use" should also be provided to industry.		✓ Reviewers should be trained on how to determine *each* term.	
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 ... that would provide the agency with the express authority to consider an off-label use, in			✓

CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
certain limited circumstances, when determining the intended use of a device under review through the 510(k) process.			
The 510(k) Working Group recommends that CDRH reconcile the language in its 510(k) flowchart (shown on page 27 of this report) with the language provided in section 513(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(i) regarding different technological characteristics and different questions of safety and efficacy.			✓
The 510(k) Working Group recommends that CDRH revise existing guidance to provide clear criteria for identifying different questions of safety and effectiveness and to identify a core list of technological changes that generally raise such questions (e.g., a change in energy source, a different fundamental scientific technology).		✓ Identifying new types of safety and effectiveness questions	
The 510(k) Working Group further recommends that CDRH develop and provide training for reviewers and managers on how to determine whether a 510(k) raises different questions of safety and effectiveness. Training on different technological characteristics and different questions of safety and effectiveness should also be provided to industry.		✓ Identifying new types of safety and effectiveness questions	
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. 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.			✓
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.			✓
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.		✓ Support guidance on use of multiples with no limitation on the number allowed.	
The Center should also explore the possibility of explicitly disallowing the use of split predicates.			✓
In addition, CDRH should update its existing bundling guidance to clarify the distinction between multi-parameter or multiplex devices (described in Section 5.1.2.3 of this report) and bundled submissions (described in Section 4.3.4.2).		✓ Only to clarify the distinction between multi-parameter or	

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
		multiplex devices	
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.	✓		
The 510(k) Working Group further recommends that CDRH conduct additional analyses to determine the basis for the apparent association between citing more than five predicates and a greater mean rate of adverse event reports, as shown in Section 5.1.2.3 of this report.			✓
The 510(k) Working Group recommends that CDRH revise existing guidance to streamline the current implementation of the de novo classification process and clarify its evidentiary expectations for de novo requests. The Center should encourage pre-submission engagement between submitters and review staff to discuss the appropriate information to provide to CDRH for devices eligible for de novo classification, potentially in lieu of an exhaustive 510(k) review. The Center should also consider exploring the possibility of establishing a generic set of controls that could serve as baseline special controls for devices classified into class II through the de novo process, and which could be augmented with additional device-specific special controls as needed.	✓		
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), what modifications are eligible for a Special 510(k).	✓		
The 510(k) Working Group further recommends that CDRH 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), and clearly explaining why each modification noted did not warrant a new 510(k). The Center could consider phasing in this requirement, applying it initially to the "class IIb" device subset described in Section 5.2.1.3, below, for example, and expanding it to a larger set of devices over time.			✓
The 510(k) Working Group recommends that CDRH consider adopting the use of an "assurance case" framework for 510(k) submissions. An "assurance case" is a formal method for demonstrating the validity of a claim by providing a convincing argument together with supporting evidence. It is a way to structure arguments to help ensure that top-level claims are credible and supported. If CDRH pursues this approach, the Center should develop guidance on how submitters should develop and use an assurance case to			✓

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
make adequate, structured, and well-supported predicate comparisons in their 510(k)s. The guidance should include the expectation that all device description and intended use information should be submitted and described in detail in a single section of a 510(k). The 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. CDRH should also develop training for reviewers and managers on how to evaluate assurance cases.			
The 510(k) Working Group further 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 allow review staff to develop a better understanding of the device□s key features. Currently, CDRH receives photographs or schematics as part of most 510(k)s; however, receiving both as a general matter would provide review staff with more thorough information without significant additional burden to submitters.			✓
Further, CDRH could include photographs and schematics, to the extent that they do not contain proprietary information, as part of its enhanced public 510(k) database, described below, to allow prospective 510(k) submitters to develop a more accurate understanding of potential predicates. Exceptions could be made for cases in which a photograph or schematic of the device under review will not provide additional useful information, as in the case of software-only devices.			✓
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.			✓
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.□			✓
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.			✓
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			✓ (See AdvaMed proposal for

CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
necessary to support a substantial equivalence determination.			subset of Class II.)
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.			✓
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.		✓ Support greater clarity of circumstances and definition of clinical data. Do not support Class IIb category. All IVD s should not be placed in Class IIb.	
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.		✓ Support exploring *current* authority	✓ Do not support *expanding* postmarket authority
The 510(k) Working Group further recommends that CDRH 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 premarket submission for future 510(k)s.		✓ Premature to consider submission of data from electronic records.	
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.		✓ Should apply to only a small subset; should be summary information only; should not include IVD products.	
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 . . .		✓ Clarify when it is appropriate to use its current authority and incorporate due process with manufacturer s input.	

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
. . . and include a discussion of pre-clearance inspections as part of its class IIb guidance.			✓ Do not support preclearance inspections.
The 510(k) Working Group recommends that CDRH develop guidance and Standard Operating Procedures (SOPs) on 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.	✓		
510(k) Working Group further recommends that CDRH enhance existing staff training on the development and assignment of product codes.	✓		
The 510(k) Working Group recommends that CDRH develop a publicly available, easily searchable database that includes, for each cleared device, a verified 510(k) summary, photographs and schematics of the device, to the extent that they do not contain proprietary information, 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.		✓ Photographs and schematics should not be included in the public database.	
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.	✓		
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. In exploring this approach, CDRH should consider options to assure that labeling could be screened efficiently, without placing a significant additional burden on review staff. For example, to allow for more rapid review of labeling changes, the Center could consider the feasibility of requiring manufacturers to submit a clean copy and a redlined copy of final labeling and subsequent updates, highlighting any revisions made since the previous iteration. As a longer-term effort, the Center could explore greater use of software tools to facilitate rapid screening of labeling changes. 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			✓

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
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.			
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.	✓		
The 510(k) Working Group recommends that CDRH continue to take steps to enhance recruitment, retention, training, and professional development of review staff, including providing opportunities for staff to stay abreast of recent scientific developments and new technologies. This should include increased engagement with outside experts, as discussed further in the preliminary report of the Task Force on the Utilization of Science in Regulatory Decision Making (described further in Section 2, below).	✓		
The 510(k) Working Group further recommends that CDRH consider establishing a Center Science Council comprised of experienced reviewers and managers and under the direction of the Deputy Center Director for Science. The Science Council should serve as a cross-cutting oversight body that can facilitate knowledge-sharing across review branches, divisions, and offices, consistent with CDRH's other ongoing efforts to improve internal communication and integration. The Science Council's role in improving the consistency of Center decisions is discussed in greater detail in the preliminary report of the Task Force on the Utilization of Science in Regulatory Decision Making.		✓	
The 510(k) Working Group recommends that CDRH develop a process for regularly evaluating the list of device types eligible for third-party review and adding or removing device types as appropriate based on available information. The Center should consider, for example, limiting eligibility to those device types for which device-specific guidance exists, or making ineligible selected device types with a history of design-related problems.			✓
The 510(k) Working Group further recommends CDRH enhance its third-party reviewer training program and consider options for sharing more information about previous decisions with third-party reviewers, in order to assure greater consistency between in-house and third-party reviews.	✓		
The 510(k) Working Group recommends that CDRH 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.	✓		
The 510(k) Working Group further recommends that CDRH periodically audit 510(k) review decisions to assess adequacy, accuracy, and consistency. The ongoing implementation of iReview (described in Section 5.3.2 of this 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		✓ Define objective of audit and authority of Council; do not support authority to reverse	

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
Council, described above, which would also oversee the communication of lessons learned to review staff, as well as potential follow-up action.		decisions.	
SCIENCE REPORT			
The Task Force recommends that CDRH revise its 2002 "least burdensome" guidance to clarify the Center's interpretation of the "least burdensome" provisions of the Federal Food, Drug, and Cosmetic Act (21 USC § 360c(a)(3)(D)(ii) and 21 USC § 360c(i)(1)(D)). CDRH should clearly and consistently communicate that, while the "least burdensome provisions" are, appropriately, meant to eliminate unjustified burdens on industry, such as limiting premarket information requests to those that are necessary to demonstrate reasonable assurance of safety and effectiveness or substantial equivalence, they are not intended to excuse industry from pertinent regulatory obligations nor to lower the Agency's expectations with respect to what is necessary to demonstrate that a device meets the relevant statutory standard.		✓ No need to revise guidance; train industry and FDA on existing guidance.	
The Task Force recommends 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), in part by developing guidance on the design of clinical trials that support PMAs and establishing an internal team of clinical trial experts who can provide support and advice to other CDRH staff, as well as to prospective investigational device exemption (IDE) applicants as they design their clinical trials. The Center should work to assure that this team is comprised of individuals with optimal expertise to address the various aspects of clinical trial design, such as expertise in biostatistics or particular medical specialty areas. The team would be a subset of the Center Science Council discussed in Section 4.2.1 of this report, and, as such, it may also serve in the capacity of a review board when there are differences of opinion about appropriate clinical trial design and help assure proper application of the least burdensome principle. CDRH should also continue to engage in the development of domestic and international consensus standards, which, when recognized by FDA, could help establish basic guidelines for clinical trial design, performance, and reporting. In addition, CDRH should consider expanding its ongoing efforts related to clinical trials that support PMAs, to include clinical trials that support 510(k)s.		✓ Include all stakeholders in development of guidance.	
The Task Force recommends that CDRH work to better characterize the root causes of existing challenges and trends in IDE decision making, including evaluating the quality of its pre-submission interactions with industry and taking steps to enhance these interactions as necessary. For example, the Center should assess whether there are particular types of IDEs that tend to be associated with specific challenges, and identify ways to mitigate those challenges. As part of this process, CDRH should consider developing guidance on pre-submission interactions between industry and Center staff to supplement available guidance on pre-IDE meetings.	✓		

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
The Task Force recommends that 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. The Center's staffing needs are discussed further below.		✓ Ensure routine work is not adversely affected; ensure oversight of team work.	
The Task Force recommends that CDRH assess and better characterize the major sources of challenge for Center staff in reviewing IDEs within the mandatory 30-day timeframe, and work to develop ways to mitigate identified challenges under the Center's existing authorities.		✓ Do not expend valuable resources; develop guidance for pre-IDE meetings.	
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.		✓ Continued validation of data owners, research contractors, study methods, and data sets.	
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.	✓		
The Task Force recommends that CDRH continue the integration and knowledge management efforts that are currently underway as part of the Center's FY 2010 Strategic Priorities. As part of these efforts, the Task Force recommends that CDRH develop more effective mechanisms for cataloguing the Center's internal expertise, assess the effectiveness of the inter-Office/Center consult process, and enhance the infrastructure and tools used to provide meaningful, up-to-date information about a given device or group of	✓		

CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
devices to Center staff in a readily comprehensible format, to efficiently and effectively support their day-to-day work.			
The Task Force recommends that CDRH, consistent with the Center's FY 2010 Strategic Priorities, develop a web-based network of external experts, using social media technology, in order to appropriately and efficiently leverage external expertise that can help Center staff better understand novel technologies, address scientific questions, and enhance the Center's scientific capabilities.		✓ Explain use of social media technology; ensure confidentiality of information; define expert selection process.	
The Task Force recommends that CDRH assess best-practices for staff engagement with external experts and develop standard business processes for the appropriate use of external experts to assure consistency and address issues of potential bias. As part of this process, the Center should explore mechanisms, such as site visits, through which staff can meaningfully engage with and learn from experts in a variety of relevant areas, including clinical care. In addition to supporting interaction at the employee level, the Center should also work to establish enduring collaborative relationships with other science-led organizations.	✓		
The Task Force recommends that CDRH develop and implement a business process for responding to new scientific information in alignment with a conceptual framework comprised of four basic steps: (1) detection of new scientific information; (2) escalation of that information for broader discussion with others; (3) collaborative deliberation about how to respond; and (4) action commensurate to the circumstance — including, potentially, deciding to take no immediate action. As it puts this approach into practice, CDRH should consider adopting several key principles. First, the process should allow for a range of individuals to participate in the deliberation phase, including managers and employees, to help take into consideration potentially cross-cutting issues and assure consistency in responding to new scientific information. To support this principle, CDRH should establish a Center Science Council, comprised of experienced employees and managers and under the direction of the Deputy Center Director for Science, to provide oversight and help assure consistency across the Center. Second, the process should be streamlined to allow for new information to be raised and addressed in a timely manner. Third, the process should include a mechanism for capturing in a structured manner the rationale for taking a particular course of action, so that it can be articulated clearly to staff and external constituencies and incorporated into the Center's institutional knowledge base. Fourth, the process should be designed to allow for prioritization of issues. The Center should also develop metrics to determine whether or not the new process is effective.		✓ Include industry in steps 3 and 4	
The Task Force recommends that CDRH enhance its data sources, methods, and capabilities to support evidence synthesis and quantitative decision making as a long-term goal.	✓		

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
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. For example, CDRH should explore 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. CDRH should also encourage industry and other constituencies to submit proposed guidance documents, which could help Center staff develop Agency guidance more quickly.		✓ Ensure use of Level 1 is limited to public health concerns	
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. Currently, manufacturers typically learn of such changes through individual engagement with the Agency, often not until after they have prepared a premarket submission. The aim of issuing a "Notice to Industry" letter would be to provide greater clarity to manufacturers, in a timelier manner, about the Center's evolving expectations with respect to a particular group of devices. Because a change in regulatory expectations would represent a change in policy, a "Notice to Industry" letter would likely be considered guidance, although it would typically be issued relatively quickly and would generally not contain the level of detail traditionally found in other guidance documents. In the interest of rapidly communicating the Center's current regulatory expectations to industry, CDRH would generally issue "Notice to Industry" letters, if such letters constitute guidance, as "Level 1 – Immediately in Effect" guidance documents, and would open a public docket in conjunction with their issuance through a notice of availability in the Federal Register. To expedite the issuance of "Notice to Industry" letters, CDRH should develop standardized templates for these letters and, as necessary, their accompanying Federal Register notices. In addition, when appropriate, CDRH should follow "Notice to Industry" letters as soon as possible with new or modified guidance explaining the Center's new regulatory expectations in greater detail and revising the guidance where necessary in response to comments received, so that external constituencies have a fuller understanding of the Center's current thinking. CDRH should also consider creating a webpage for identifying and explaining new information that has altered the Center's regulatory expectations, so that, across all CDRH-regulated products, external constituencies can better understand the rationale for changes in the Center's requirements.		✓ Clearly define circumstances for use; establish implementation timeframes; make NIT public, not limited to current manufacturers	
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			✓

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CDRH RECOMMENDATION	SUPPORT	SUPPORT WITH MODIFICATION	DO NOT SUPPORT
described in greater detail in the preliminary report of the 510(k) Working Group (described further in Section 3, below).			
The Task Force recommends that CDRH 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. The SOP should include the expectation that when a decision is made to take a particular course of action, including a change in evidentiary expectations, the action and its basis should be communicated clearly and promptly to all affected parties. If it is not possible to provide complete detail about the basis for an action due to confidentiality concerns, Center staff should share as full an explanation as is allowable and state why a more complete explanation is not permissible. In addition, Center leadership should take steps to make sure that all employees have an accurate understanding of what information they are permitted to discuss with manufacturers, so that information that would help clarify the basis for a particular action is not needlessly withheld.		✓ Involve all stakeholders in developing the procedure	
The Task Force recommends that CDRH continue its ongoing efforts to make more meaningful and up-to-date information about its regulated products available and accessible to the public through the CDRH Transparency Website, consistent with the Center's FY 2010 Strategic Priorities and the work of the FDA Transparency Task Force. In addition to the pre- and postmarket information that is already available on CDRH Transparency Website, the Center should move to release summaries of premarket review decisions it does not currently make public (e.g., ODE 510(k) review summaries) and make public the results of post-approval and Section 522 studies that the Center may legally disclose. Making such information readily available to the public will provide CDRH's external constituencies with greater insight into the data that guide the Center's decisions and evolving thinking.		✓ Do not post decisions of devices that were not cleared.	

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Specific Comments

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.*

"Same Intended Use"

Lack of a Clear Distinction between Terms

Recommendation: *The 510(k) Working Group recommends that CDRH 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. Several public comments expressed concern that, if these two terms were combined, any proposed change in a device's label indications could be considered a change in "intended use." The Working Group recognizes the importance of providing submitters with the flexibility to propose certain changes to their labeling, without such a change necessarily constituting a new "intended use." Therefore it recommends that CDRH carefully consider what characteristics should be included under the term "intended use," so that modifications that are currently considered to be only changes in "indications for use" and that CDRH determines do not constitute a new "intended use," are not in the future necessarily construed as changes in "intended use" merely because of a change in semantics. Any change in terminology would be intended to provide greater clarity and simplicity, not necessarily to make the concept of "intended use" more restrictive. The Center should also carefully consider what it should call the existing "Indications for Use" statement in device labeling and the "Indications for Use" form currently required for all 510(k)s, in order to avoid confusion in terminology but still maintain an appropriate level of flexibility for submitters.*

AdvaMed does not support the consolidation of "intended use" and "indications for use" into a single term, and maintains that there is value in preserving these terms as separate concepts because the terms are not synonymous. It is critical that the two concepts remain distinct and separate, as they clearly serve different purposes. "Intended use" broadly describes the use of a generic type of device (i.e., what the device does) while "indications for use" more specifically describes the device's clinical uses and patient population(s). Combining the two terms may constrain the meaning of intended use, remove the flexibility that is currently afforded to the Agency in determining what new uses should be regulated within the confines of Section 510(k), and unnecessarily narrow the meaning of substantial equivalence. Indeed, combining the terms eliminates the distinction between "general" and "specific" uses that FDA has relied upon in determining whether the addition of a specific indication for use may trigger the need for additional data, including clinical data, versus the need for a PMA or a *de novo* classification.[2]

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[2] *See* FDA Guidance for Industry: General/Specific Intended Use (1998). Available at: http://www.fda.gov/MedicalDeviceRegulationandGuidance/GuidanceDocuments/ucm073944.htm.

FDA has recognized that the addition of a specific indication may or may not alter a device's intended use, depending on a multitude of factors. Furthermore, removing the "Indications for Use" terminology from its tool box will result in confusion among patients and health care professionals who rely on the indications for use appearing in product labeling consistent with other FDA-regulated products. If, however, FDA determines that the intended use is altered, it will issue an NSE determination. FDA needs to retain the flexibility of considering those factors. From a patient perspective, we are concerned that patient access to new devices would be delayed because of a potential increase in Not Substantially Equivalent (NSE) determinations resulting from a combination of these two terms.

AdvaMed believes that the specific differences between the terms, "intended use" and "indications for use," can be clarified by developing definitions of each concept within the context of substantial equivalence. The Code of Federal Regulations (21 C.F.R. § 801.4) provides a definition of intended use in the context of postmarket behavior related to the need for adequate directions for use as described in 21 C.F.R. § 801.5, and indications for use is defined in the PMA regulations (21 C.F.R. § 814.20). Neither is defined for use in the context of substantial equivalence. With that in mind, AdvaMed recommends adding definitions in 21 C.F.R. Part 807 that clarify the use of these terms in the premarket notification context.

AdvaMed recommends amending 21 C.F.R. Part 807 to include a discussion of intended use and indications for use. We suggest that the following section be added to Part 807:

> **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. *Intended use* is constructed to encompass the appropriate breadth of use for which the regulatory controls for the 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 by the persons legally responsible for the proposed labeling of the device that is the subject of the premarket notification submission. *Intended use* describes what the device is intended to provide to the user and patient and for what purpose. 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.[3] *"Indications for use"* provides a detailed, specific description of the specific target population(s) for the intended use that generally describes device function, and includes the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, and/or a description of the general or specific patient populations or anatomies for which the device is intended, as appropriate.**

[3] This aspect of our proposed definition of intended use derives from Section 513(i)(1)(E)(1) of the Act, which states that "[a]ny determination by the Secretary of the intended use of a device [for the purpose of determining substantial equivalence] shall be based upon the proposed labeling submitted in a report for the device under Section 510(k)."

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AdvaMed supports the development of guidance documents that *clarify* the meanings of "intended use" and "indications for use," rather than revising existing guidance to consolidate these terms, as recommended by the 510(k) Working Group. Examples distinguishing intended use from indications for use that could be provided in future guidance documents include:

- The *intended use* of an electrosurgical cutting and coagulation device is to remove tissue and control bleeding by use of high-frequency electrical current (21 C.F.R. §878.4400). Electrosurgical cutting and coagulation devices, however, may be specifically designed to accommodate different anatomies. They may have *indications for use* in thoracic, gynecologic, ENT, or other procedures, as illustrated by the 31 product classification codes for electrosurgical instruments.

- The *intended use* of an infusion pump is to deliver fluid to a patient in a controlled manner (21 C.F.R. §880.5725). External infusion pumps may have any of the following *indications for use*:
    - general administration of drug solutions vs. blood vs. insulin.
    - intravenous, epidural, subcutaneous, subarachnoid, etc.
    - patient-controlled analgesia
    - hospital versus home use

- The *intended use* of a gas analyzer is to provide a means of monitoring gas concentration and to alert clinical personnel when limits fall outside of a pre-specified range (there are over 15 classification regulations for gas analyzers). The indications for use of a gas analyzer could be for an anesthetic agent, or oxygen, carbon dioxide, or nitrous oxide.

AdvaMed notes that not all devices subject to 510(k) have both an intended use and an indication for use (e.g., a syringe delivers whatever liquid it contains, what it delivers is not specified, and there is no specific patient population). Also with respect to intended use, AdvaMed recommends that FDA take into consideration that intended use for *in vitro* diagnostic devices may include what is being measured, and for what purpose. However, the intended use should not extend to an IVD's particular performance characteristics (e.g., accuracy, ranges, or cut-off values).

AdvaMed also 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 have been accepted by FDA. Because of the significant impact of any modifications to the definitions of intended use and indications for use, we believe it is necessary for the Agency to provide notice and an opportunity for public comment.

AdvaMed supports the Working Group's recommendation that the Indications for Use statement (if any) be included in the *labeling* but that it should not be provided directly on the package *label*. Further, some packages are not sized to contain this information and there is an environmental issue associated with increased packaging. This requirement would necessitate

the amendment of 21 C.F.R. Part 801, requiring notice and comment. Users are provided with the product labeling, which already contains the Indications for Use.

Insufficient Guidance for 510(k) Staff and Industry

Recommendation: *The 510(k) Working Group recommends that CDRH develop or revise existing guidance to clearly identify the characteristics that should be included in the concept of "intended use."*

AdvaMed supports the revision of existing guidance to clarify the terms "intended use" and "indications for use," but does not support the recommendation to consolidate these terms.

Recommendation: *The 510(k) Working Group further recommends that CDRH provide training for reviewers and managers on how to determine "intended use." Such training should clarify the elements of a device application that should be considered when determining the "intended use," e.g., product labeling, device design (explicit or implied), literature, and existing preclinical or clinical data. Training on "intended use" should also be provided to industry.*

If FDA adopts AdvaMed's recommended definition of "intended use" and "indications for use," then FDA should conduct training of review staff on to determine these terms.

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 ... 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.*

AdvaMed does not support this recommendation. AdvaMed does not agree with granting additional authority to FDA when the Agency believes that a device's primary intended use is an off-label use that is not reflected in the proposed labeling. FDA currently has statutory authority to act on off-label use that could cause harm by requiring a statement in the product labeling.

Congress has previously addressed this issue. In the Food and Drug Administration Modernization Act of 1997 (FDAMA), Congress clearly defined the approach the Agency must take when identifying concerns regarding potential off-label use of devices undergoing 510(k) review. This approach, codified at Section 513(i)(1)(E)(i) of the Act,[4] provides that the

[4] Section 513(i)(1)(E)(i) of the Act provides that "[a]ny determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under Section 510(k). However, when determining that a device can be found substantially equivalent to a legally marketed device, the director of the organizational unit responsible for regulating devices (in this subparagraph referred to as the "Director") may require a statement in labeling that provides appropriate information regarding a use of the device not identified in the proposed labeling if, after providing an

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Agency's determination of intended use "shall be based upon the proposed labeling," but that the Agency may address concerns about potential off-label use through requiring a statement in the labeling, after consulting with the applicant and if the following criteria are met: if 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 if such use could cause harm.

We do not believe that there is a need for any further restrictions on 510(k) clearance related to potential off-label use. A properly administered 510(k) program ensures that devices receiving FDA clearance are suitable for the intended use and indications for use in the proposed labeling for which they are being cleared. The determination of substantial equivalence should not take into account potential off-label uses, and clearance should not be withheld for the requested use pending submission of data for a suspected off-label use that the sponsor has not requested. Instead, the statute directs CDRH to address those concerns by requiring statements in the labeling, including limitations within the intended use statement -- without otherwise affecting a substantial equivalence determination. This Congressionally-mandated path provides a more flexible path for CDRH to follow while protecting public health, and is less onerous for both the Agency and industry.

AdvaMed does not support the expansion of FDA's authority to consider an off-label use as the primary intended use. This expanded authority would place reviewers in the untenable position of second guessing the sponsor's intentions and would be disruptive to the 510(k) program. Further, a 510(k) could automatically receive an NSE determination if the sponsor has not provided data on what FDA presumed to be the primary use, thereby leading to an NSE decision for the legitimate 510(k) use requested by the sponsor.

Companies with the intent to market a device for a legitimate intended use should not be prevented from obtaining 510(k) clearance because other product uses may exist. In fact, in a unanimous decision, the United States Supreme Court has acknowledged the importance of off-label use in *Buckman v. Plaintiffs' Legal Committee*, No. 98-1768, stating that, "'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." Further, the possibility of a CDRH decision to require a company to support an additional intended use may result in the company's decision not to pursue commercial development of a new and potentially useful device or diagnostic, further stifling innovation. Additionally, such a requirement could represent an undue hardship to a smaller company that does not have the economic means to pursue a use it did not intend.

As noted above, where CDRH has concerns that there is a reasonable likelihood that the device will be used outside of the proposed labeling and when that use potentially could cause harm, it

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opportunity for consultation with the person who submitted such report, the Director determines and states in writing "(I) that 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 (II) that such use could cause harm."

now issues an SE with limitations decision and requires manufacturers to include adequate warnings against such use in the labeling. Likewise, in the postmarket period, the Agency has the ability to deal with manufacturers that engage in off-label promotional activities. Specifically, 21 C.F.R. 801.4 provides the Agency with considerable discretion in identifying off-label uses and company activities geared toward off-label promotion. When these situations arise, FDA can take many actions to stop off-label promotion and to encourage compliance with applicable requirements.
When substantial off-label use is discovered in the postmarket period and the company has not illegally promoted such use, FDA should encourage companies to seek clearance for the off-label use and to develop adequate directions for use for these new clinical applications, or to add or maintain a specific limitation in labeling for the device. In instances where the company wishes to include the off-label use(s), FDA should work with the company to identify the type of data required to support an expanded use.

Different Questions of Safety and Effectiveness

Inconsistent Terminology

Recommendation: *The 510(k) Working Group recommends that CDRH reconcile the language in its 510(k) flowchart (shown on page 27 of this report) with the language provided in section 513(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 360c(i) regarding "different technological characteristics" and "different questions of safety and efficacy."*

AdvaMed does not support the 510(k) Working Group s recommendation that the language in FDA s 510(k) flowchart and the statutory language in 513(i) of the Act be reconciled. As reflected in Blue Book memorandum K86-3, the Agency has interpreted different questions to be new types of questions. AdvaMed believes that the current wording in the flowchart fits within the intent of the statute. It is a long-standing and well-established interpretation that has worked well for many years. By inserting the words new types, it is our understanding that the Agency was indicating that different questions can be grouped in a manner that provides FDA appropriate discretion in deciding what scientific questions justify making a new device NSE on this basis. As a result, any modification of this well-established approach is a new interpretation, which requires notice and comment.

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Insufficient Guidance for 510(k) Staff and Industry

Recommendation: *The 510(k) Working Group recommends that CDRH revise existing guidance to provide clear criteria for identifying "different questions of safety and effectiveness" and to identify a core list of technological changes that generally raise such questions (e.g., a change in energy source, a different fundamental scientific technology).*

AdvaMed supports the Working Group's recommendation for clear guidance, subject to notice and comment, focused on the use of risk assessments in identifying potential "new types" of safety and effectiveness questions. The use of flowcharts differentiating elements for consideration would further clarify the process.

Recommendation: *The 510(k) Working Group further recommends that CDRH develop and provide training for reviewers and managers on how to determine whether a 510(k) raises "different questions of safety and effectiveness." Training on "different technological characteristics" and "different questions of safety and effectiveness" should also be provided to industry.*

AdvaMed supports the Working Group's recommendation to train reviewers and managers on "new types of safety and effectiveness questions." Training should be provided to reviewers, managers, and industry so that all understand that when questions are raised by a new technology, and they can be answered by established and/or recognized standards, or established, recognized, or validated test methods, then an NSE determination is not the automatic result. AdvaMed further recommends that CDRH focus on clarifying which questions of safety and efficacy are "different," or "new types," rather than on the underlying device technology and its characteristics.

AdvaMed believes that a question of safety and effectiveness is not "different" if the question can be answered through established, well recognized, or validated test methods. Advances in materials science provide examples of how specific scientific questions can be approached in the context of SE decision-making. In the medical device industry, manufacturers constantly search for new materials. As new materials are identified, questions often arise regarding their suitability for a particular use. While the use of a new material in a device may raise questions, historically FDA has considered the question to be of the same "type" that previous materials have raised and, therefore, have not generally viewed changes in materials as a justification for a NSE decision. As an alternative to considering which questions are of the same type and which are not, focusing on what testing is required to address the question, and whether the testing involves well established and recognized methods removes much of the subjectivity. In the context of the latest materials science, questions regarding a new material's ability to meet the demands of a particular use environment can usually be addressed through bench and animal testing.

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.*

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Concerns about Predicate Quality

Recommendation: *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. 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.*

AdvaMed does not support the Working Group's recommendation that CDRH develop guidance on when a device should no longer be available for use as a predicate. AdvaMed believes that statutory change is required to disqualify a legally marketed device from being available for use as a predicate because of purported safety or effectiveness concerns, and cannot be accomplished by guidance. AdvaMed does not believe, however, that it is necessary to promulgate new legislation, as FDA already has the authority to remove violative devices from the market. Under Section 513(i)(2) of the Act, those devices that have been removed from the market by FDA or have been determined adulterated or misbranded by a judicial order are disqualified from being predicate devices. Simply put, guidance documents cannot create requirements and cannot supersede statutory law. CDRH's current statutory remedy to a device that it believes is unsafe or ineffective is to bring an enforcement action to remove the device from the market (i.e., the Agency may ban the device). In addition, if the controls for assuring safety or effectiveness are inadequate, CDRH can develop special controls or reclassify the device. Using guidance to shortcut the statute is without legal basis and unacceptable.

The 510(k) Working Group's concerns appear not to be relevant to 510(k)s reviewed by the Office of *In Vitro* Diagnostics (OIVD). OIVD informs companies of the product or technology to which the 510(k) device must be compared (gold standard: e.g., bacteriological media/culture for many infectious diseases), thereby reducing the risk of safety and effectiveness concerns with the predicate device(s).

AdvaMed further notes that 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. AdvaMed also notes that devices evolve as new technological advances are made, and are not expected to be identical to the older predicate devices. For example, if FDA has concerns about the safety and effectiveness of a legally marketed device, those concerns may not apply to the 510(k) device because of technological improvements, and FDA has full statutory authority to require evidence that the technological characteristics of the new device do not raise new/different safety and effectiveness concerns. Finally, AdvaMed notes that not all devices are removed from the market because of reasons that would disallow their use as a predicate (i.e., safety and effectiveness concerns). For example, companies will discontinue a product line for business reasons unrelated to safety and effectiveness.

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Rescission Authority

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.*

AdvaMed does not support the issuance of a regulation to exercise rescission authority nor does AdvaMed support expansion of rescission authority. AdvaMed believes that, absent the commission of an act of fraud in establishing the substantial equivalence of a device, rescission would not be justified and should not be allowed, because of the "domino effect" it could have. If FDA had the authority to rescind a 510(k) for reasons other than fraud, the legal marketing status of each device that had subsequently relied on the rescinded device as a predicate would be jeopardized (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. Expanding FDA's 510(k) rescission authority to include rescission based on safety or effectiveness concerns is not only unnecessary, it also would cause more harm than good for several reasons. The 510(k) clearance system is a classification process and is based on predicates. Once a device is cleared and FDA has made the decision that its design and intended use are substantially equivalent to a predicate device, FDA should not rescind that decision because, for example, a device is manufactured under poor conditions that impair its safety or effectiveness or because a manufacturer has changed the device's design. If a predicate, key to a line of subsequent devices, is rescinded, it could result in each and every device that cites the rescinded device being rescinded as well, even when those devices do not share whatever defect occurred in the rescinded device, with a potentially significant impact to public health. As noted above, FDA currently has the tools to isolate a device that violates any part of the Act, is determined not to be substantially equivalent to a predicate, or is not safe and effective to protect the public health without creating unreasonable jeopardy for innocent parties.

The Act provides FDA with numerous tools to remove violative devices from the market and should not accomplish it in a way that may broadly limit access to safe and effective medical devices, thus undermining the public health. If a device is considered unsafe because it is manufactured under noncompliant GMPs, is manufactured incorrectly, or the manufacturer has changed the design without meeting the appropriate 510(k) premarket requirements, then that device should be appropriately dispositioned per FDA's current postmarket authorities provided in the Act. These authorities include reclassification, recall, warning letters, and other enforcement actions. In addition, the Act already provides for the banning of a medical device in situations of substantial deception or unreasonable and substantial risk of illness or injury.[5] Banned medical devices can no longer be legally marketed and can therefore not be cited as a predicate device. FDA also has the authority to issue an order for mandatory device recall[6] or to

[5] See Section 516 of the Act

[6] See Section 518 of the Act

reclassify a device.[7] FDA also may, when necessary, obtain court orders for product seizure. These conditions can be remedied, however, and should not be used as grounds for revoking the original 510(k) decision, because the currently available statutory tools enable the Agency to protect the public health and also maintain the integrity of the classification system.

AdvaMed agrees that FDA can nullify a substantial equivalence determination, if the 510(k) submitter procured the determination through fraud, or if the Agency made an inadvertent administrative mistake or error and corrected it prior to the order becoming final. Rescinding one 510(k) clearance could potentially reclassify a group of devices, and FDA does not need to take such action in order to protect the public health. The Act provides the Agency with numerous efficient means to remove unsafe or violative devices from the market. Moreover, the Act authorizes FDA to reclassify devices based on new information, including reassessment of past information in the administrative record.

In summary, FDA does not have express or implied statutory authority to rescind 510(k) classification determinations, nor are there compelling policy grounds to do so. The Working Group indicated that rescission would be seldom used in response to particular circumstances; we believe the law now provides adequate remedies for any such circumstance and fully provides adequate protection of the public health if the Agency is willing to use the remedies Congress gave it to ensure safe and effective devices. Outside of the limiting circumstances described above, undermining the predicate status of a device through rescission would not advance the public health and would undermine the entire classification system set forth in the Act.

Please see the detailed legal analysis of FDA's proposed expanded rescission authority provided in Attachment B.

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 also explore the possibility of explicitly disallowing the use of "split predicates." In addition, CDRH should update its existing bundling guidance to clarify the distinction between multi-parameter or multiplex devices (described in Section 5.1.2.3 of this report) and bundled submissions (described in Section 4.3.4.2).*

AdvaMed is opposed to disallowing the use of split predicates and supports the use of multiple predicates. The current bundling guidance works well for bundled submissions, and the only revision necessary is to clarify the distinction between multi-parameter or multiplex devices. AdvaMed supports updating CDRH's existing bundling guidance only to clarify the distinction between multi-parameter or multiplex devices. AdvaMed believes that the use of multiple

[7] See Section 513(e) of the Act.

predicates, i.e., using more than one predicate where each predicate individually supports substantial equivalence, 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. Further, disallowing the use of "split predicates" and/or arbitrarily disallowing the use of more than five predicates for a given device under 510(k) review could result in an unnecessary burden on the PMA and *de novo* submission programs for both CDRH and industry, resulting in delayed or no patient access to new devices. The bases for our positions are detailed below.

"Split" Predicates

In its August report, FDA defined "split" predicates as taking the intended use from one device and the technology from another device and putting those two together to try to reach a substantial equivalence determination. Per statute, the new device must always have the same intended use as the predicate device. Different technology is permissible provided that the different technology does not raise new or different types of questions. First and foremost, and as noted above, AdvaMed opposes disallowing the use of "split predicates." Such an action will stifle innovation and evolutionary change in device design, which the 510(k) program was designed to encourage.

The use of split predicates is a reasonable approach to showing substantial equivalence. We believe the use of a split predicate is vital to innovation and to the public health goals of the 510(k) program because many devices are modular in nature (i.e., they are made up of a combination of components). AdvaMed believes that FDA should allow the submission of 510(k)s in accordance with actual product configuration, enabling the use of split predicates where appropriate.

In cases where split predicates are used, the 510(k) sponsor should be required to provide risk-based justification for using split predicates for their particular device. This risk-based approach is consistent with the concepts behind "multiple predicates" and the dual goal of CDRH to protect public health while encouraging device innovation. Guidance documents should include CDRH's current thinking on acceptable risk-based justifications to encourage high-quality 510(k) filings. Further, reviewers should be trained on the use of split predicates.

Split predicates add to the dataset for FDA to consider in a useful manner. While there is often a "core" predicate based on intended use or mode of action, it may not seem comparable owing to a different feature such as power source, materials, or technology. Being able to demonstrate to FDA that there is marketing experience to be drawn upon for this different feature allows FDA to consider all of the available information and make an informed judgment as to the level of risk introduced by the new product.

Please note that the IVD practice of providing performance data against both a "gold standard" and a predicate is not the same as the use of split (or multiple) predicates. The data from the reference method, or gold standard, are meant to provide additional information on the IVD's

accuracy as compared to a recognized method, not to demonstrate substantial equivalence. The predicate is used to demonstrate substantial equivalence.

Multiple Predicates

Since 1986, the Agency has recognized the concept of multiple predicates in cases where new devices and multiple predicates have compatible intended uses. Specifically, in a 1986 guidance,[8] FDA stated that a new device made up of a combination of devices of different types and classifications could be substantially equivalent to multiple predicates; however, the classification of the new device would be that of the highest classification of the predicates relied upon to show substantial equivalence. By extension, multiple predicates for new devices within the same generic type are permissible and consistent with FDA's longstanding interpretation of its premarket notification classification provisions.

AdvaMed supports the development of guidance for use of multiple predicates, but does not support any guidance that arbitrarily restricts the number of predicate devices that can be used. FDA should expect a 510(k) submission to provide a clear demonstration of safety and effectiveness, and that the aggregate of the components does not create new or different questions of safety or effectiveness. To curtail such an approach would, in some cases, require multiple, step-wise 510(k)s that would significantly delay introduction of more practical technology and would burden the review system with unnecessary 510(k)s.

Even if FDA were to eliminate the ability for 510(k) submitters to rely on multiple predicates, new devices that incorporate features of more than one legally marketed Class I or Class II device could still be classified into either class under the *de novo* process and could then serve as predicates for subsequent devices. The *de novo* classified device could then serve as a predicate for each of the predicates that would have been cited if a multiple predicate approach had been allowed. In other words, changing the Agency's historical use of multiple predicates elevates form over substance and fails to advance the public health while creating extra work and protracted timelines for FDA and industry.

More than Five Predicates

As noted above, AdvaMed also opposes the Working Group's proposal to prohibit more than five predicate devices. As noted by the Working Group, multiplex devices could represent more than five predicate devices' functionality. Indeed, some innovative technologies, like microarrays, could require well over the five-predicate limit. Furthermore, as devices become more complex and attempt to combine more features for both convenience and economy, the need to reference multiple predicates will increase. 510(k) sponsors should be provided the opportunity to propose and justify within the submission the use of multiple predicate devices. The effect of limiting the number of predicates could result in multiple 510(k)s where one submission would have sufficed, putting further pressure on scarce FDA resources.

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[8] *Guidance on the Center for Devices and Radiological Health's Premarket Notification Program* (*Blue Book Memo. #K86-3*) (June 30, 1986) at 13.

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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.*

AdvaMed supports reviewer training on submissions with multiple predicates, and on the current bundling guidance. We further recommend that similar training be offered to the manufacturing community to ensure high-quality, consistent 510(k) submissions for CDRH to review. AdvaMed offers to partner with CDRH to conduct workshops to disseminate such training to the medical device manufacturing community.

Also, please note that, bundling is a useful and efficient submission and review method, particularly in the IVD arena. For example, if a manufacturer of diagnostic instruments makes a change to a family of instruments, CDRH can review the change only once, instead of multiple times. Likewise, a reagent for use on multiple instruments within a family could be adequately reviewed once. For IVDs, for which a Pre-IDE meeting that discusses the content of the bundled submission has been held, a well-written single 510(k) can be efficiently reviewed and cleared within the current 90-day performance goal.

Recommendation: *The 510(k) Working Group further recommends that CDRH conduct additional analyses to determine the basis for the apparent association between citing more than five predicates and a greater mean rate of adverse event reports, as shown in Section 5.1.2.3 of this report.*

AdvaMed does not support the analyses proposed by the Working Group because we believe that there is no basis to correlate adverse event data to the number of predicates in a submission, as the Working Group did in their report. FDA is implying that it has the ability, through the 510(k) process, to reduce the mean rate of adverse event reports by reviewing several step-wise 510(k)s for a product with multiple predicates, rather than one 510(k) for a product with multiple predicates. AdvaMed does not understand this reasoning, as submission and clearance of 510(k)s are based on data and evidence, which should be the same whether multiple 510(k)s or a single 510(k) is submitted.

Regarding the greater mean rate of adverse event reports for devices with multiple predicates, we recommend that a formal investigation and determination of root cause of the adverse event be undertaken before inferring that the 510(k) process is responsible.

Recommendation: *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 from eligible devices.*

Recommendation: *The 510(k) Working Group recommends that CDRH revise existing guidance to streamline the current implementation of the de novo classification process and clarify its evidentiary expectations for de novo requests. The Center should encourage pre-submission engagement between submitters and review staff to discuss the appropriate information to provide to CDRH for devices eligible for de novo classification, potentially in lieu of an exhaustive 510(k) review. The Center should also consider exploring the possibility of establishing a generic set of controls that could serve as baseline special controls for devices classified into class II through the de novo process, and which could be augmented with additional device-specific special controls as needed.*

AdvaMed strongly supports (1) revision of existing guidance on the *de novo* classification process; (2) pre-submission meetings to discuss data requirements for a *de novo* classification; and (3) a generic set of special controls that can be augmented with device-specific special controls as needed. Strengthening and optimizing the *de novo* process through a well-defined regulatory pathway will benefit the Agency, industry, and patients. This under-utilized 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. Indeed, if CDRH were to adopt a risk-based approach, some products that are currently subject to PMA could potentially be more efficiently and effectively reviewed through the *de novo* process.

AdvaMed recommends that FDA eliminate the need to submit a 510(k) and receive an NSE determination before requesting *de novo* down-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 (i.e., a "Pre-IDE"), where FDA and the sponsor agree to use of the *de novo* process as a viable pathway as well as to the content requirements of the *de novo* submission. Early utilization of a scientific panel of experts, when needed, could benefit this pre-review. We suggest that the sponsor requesting the *de novo* classification provide completed hazard analyses in the "Pre-IDE" document and a decision-making matrix, or algorithm, using FDA-recommended templates, which could be based on current ISO 14971. The content of the *de novo* should include supportive evidence to allow the Agency to fully evaluate the risks and benefits of the device. Clinical trials or clinical data should not be an automatic requirement of a *de novo* submission; however, the hazard assessment and decision-making matrix should clearly document whether these studies are required.

AdvaMed recommends that the existing guidance for assessing the eligibility of devices for *de novo* review be revised to include the following information:

1. A determination of whether the device has a different intended use or the same intended use but has new technology as compared to the named predicate device(s) that raises different questions of safety and effectiveness.

2. A hazard analysis and Special Controls document template, including reference to ISO 14971 - *Medical devices -- Application of risk management to medical* devices *for assessing the types of risks associated with new technologies or those associated with a new intended use.*
3. A flowchart with key decision criteria (similar to the flowchart used in "Deciding When to Submit a 510(k) for a Device Undergoing a Change" guidance). We note that OIVD already employs the use of a similar flow chart.
4. We suggest that the flowcharts include the following (this list is not inclusive):
   a) Is the device a prescription device, over-the-counter (OTC), or point-of-care (POC) device?
   b) Are there existing clinical data on the use of this device (e.g., outside of the U.S.)?
   c) Identify any hazards that the device poses to individual or public health.
   d) Identify the probability of harm.
   e) Does the device directly diagnose a particular disease or condition or is the device used in conjunction with other tests to establish an overall understanding of the clinical condition of patient?
   f) What is the likelihood that the device could malfunction or the malfunction could be undetected?
   g) What is the severity of harm if the device malfunctioned or was misused? Are there general or specific controls available to reduce the likelihood or severity of the malfunction? What are they?
   h) Will a new special control guidance document reduce the likelihood or severity of harm?
   i) If, with special controls, the likelihood of the malfunction to occur is high, and the severity of harm is high (death or serious injury), then not eligible for *de novo* classification.
   j) If special controls will significantly reduce the likelihood of malfunction and greatly limit severity of injury, then review as *de novo*.

As identified in FDA's 510(k) report, a generic set of special controls for devices reviewed under the *de novo* process could be a good step to strengthening and streamlining the process and providing clear parameters at the outset. A generic set of special controls more like the essential principles of the Global Harmonization Task Force (GHTF) would provide a means to create a consistent evidentiary standard for *de novo* reviews, and would minimize movements toward the full PMA set of requirements "as is appropriate because the *de novo* process was intended to be an alternative process for FDA to classify the device into Class I or Class II. To increase consistency in the process, we recommend the creation of a template identifying these generic special controls, as well as consideration of a standard submission format similar to the Global Harmonization Task Force Standard Technical Document (GHTF STED) format. Moreover, to the extent these generic special controls replace the product-specific special controls currently required under the *de novo* process, we encourage CDRH to publish detailed decision summaries

that provide industry with sufficient detail to understand CDRH's specific thinking related to specific devices. Further, to increase the efficiency of the *de novo* process, we recommend clear guidance on how to effectively use a Pre-IDE meeting in the context of the *de novo* process. As noted previously, elimination of the current process of having to file a 510(k) and receive an NSE determination as a pre-requisite to filing a *de novo* request would streamline the process considerably.

Again as noted in FDA's report, we agree there is merit in minimizing the time spent on the 510(k) review for a product that clearly is *de novo*. The review should focus on what in addition may be needed for the next level review. The evidentiary expectations for classification should be clearly communicated to the applicant, including the use of pre-submission meetings, where appropriate. The use of a generic set of special controls more like the GHTF principles would assist in focusing and clarifying this process.

Lastly, because of the importance of developing this pillar of FDA's regulatory framework, we recommend the Agency consider holding a public meeting on this process and working with the industry and other stakeholders to optimize this process.

2. Well-Informed Decision Making

RECOMMENDATION: *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.*

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), what modifications are eligible for a Special 510(k).*

AdvaMed supports the recommendation to update the existing guidance (K97-1) to clarify what types of modifications do or do not warrant submission of a new 510(k). While we agree this guidance is due for a review/update, this is a good guidance that has proved useful to FDA and industry over the years. At CDRH's request, AdvaMed submitted suggestions for improvements to the guidance in May 2010. We noted that the use of flow charts to assess changes has been especially helpful and provided input on what areas needed clarification. Consideration of the risk evaluation process as a means to assess changes rising to the level of a new filing is recommended.

The 510(k) Working Group, in its description of the history of Section 510(k), describes the implementation of the New 510(k) Paradigm. In addition to the information provided in the Preliminary Report, it is important to recognize that the 510(k) Paradigm was introduced at a period in time when the CDRH review process had slowed down to such a degree that serious concerns were raised that public health was not being promoted and innovation was being stifled. In response, CDRH developed a number of means, of which the Special 510(k) was one, to obtain essential information on device modifications, while imposing the least possible burden on industry and the Agency to enable protection of the public health. It also is noteworthy that FDA received the Hammer Award for Re-invention of Government from the Clinton Administration, in recognition of the importance and value of this initiative. AdvaMed believes the current process has merit; that it adequately protects the public health while encouraging innovation.

In support of its recommendation to identify the modifications that are eligible for a Special 510(k), the FDA Working Group cites Medical Device Report (MDR) data from CDRH's databases that suggest the MDR rate for devices that were cleared through the Special 510(k) process is slightly higher than for Traditional or Abbreviated 510(k)s. As noted, CDRH believes that the total number of MDRs likely is under-reported and that MDRs frequently do not cite the 510(k) number of the device associated with the adverse event. The conclusion reached is that further analysis would need to be conducted. AdvaMed believes it is premature to reach any conclusion about the effectiveness of the Special 510(k) or limiting the devices whose modifications are eligible for Special 510(k).

AdvaMed does not agree that the MDR data accurately reflect the Special 510(k) process. FDA has recognized that the reporting system, as good as it is, is limited. Likewise, information presented by Professor Ralph Hall to the Institute of Medicine (IOM) for its review of the 510(k) process indicates that MDR data are not good tools to judge performance of the 510(k), for the following reasons: highly variable reporting rates, reporting of inaccurate information, reporting of unconnected events, lack of quality control, and lack of confirmation. Hall suggests that recall information may be a better indication.

Professor Hall, in his assessment of the 510(k) process, looked at the relationship between Class I recalls and 510(k)s. He found that only 0.22% of Class I recalls were associated with 510(k) and related to premarket issues. Professor Hall did not find a relationship between Special 510(k) and Class I recalls. Interestingly, he found a similar rate of Class I recalls for devices subject to Premarket Approval. Dr. William Maisel, formerly of the Medical Device Safety Institute at the Beth Israel Deaconess Medical Center, who also looked at recalls, found a slightly higher rate of recalls associated with devices subject to Special 510(k)s. Combined with Professor Hall's data, this would indicate that the higher rate of recalls for devices subject to a Special 510(k) were not Class I recalls, but Class II or III recalls, representing moderate or minimal risk to public health. A report commissioned by AdvaMed and conducted by the Battelle Institute (Attachment A), confirms that the risk of recall related to use of the Special 510(k) process is not significantly higher than 510(k) products cleared through relative to CDRH's other review pathways.

As noted above, there are definite benefits associated with the use of the Special 510(k), most importantly the appropriate allocation of FDA resources for review of minor modifications to manufacturers' own devices. Design control requirements ensure that companies perform and document a thorough analysis of risks and potential risks associated with a specific device and have risk management programs to mitigate all risks. Companies also have a great deal of information, including information available to FDA, regarding the prior generations of the device. This information is used as inputs into the design control process. All of the information within the Design History File is available to FDA during routine inspections of manufacturers and FDA can, if needed and it is germane to the issue of substantial equivalence, request this information as part of any premarket review process. However, either limiting the scope of the Special 510(k) process or routinely requesting this information could impose an unnecessary burden on CDRH and the industry, without any corresponding benefit.

Recommendation: *The 510(k) Working Group further recommends that CDRH 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), and clearly explaining why each modification noted did not warrant a new 510(k). The Center could consider phasing in this requirement, applying it initially to the "class IIb" device subset described in Section 5.2.1.3, below, for example, and expanding it to a larger set of devices over time.*

AdvaMed does not support this recommendation for all Class II devices. This recommendation by the Working Group does not address the fundamental root causes identified in the discussion of unreported device modifications leading to the Working Group's recommendation. The examples cited, such as misuse of the Special 510(k) process, are more appropriately addressed within the Agency's current guidance, specifically the conversion of Special 510(k)s to Traditional 510(k)s, and compliance enforcement actions for extreme cases, as described in the Case Study: Unreported Modifications (pp 68-69).

The recommendation may be appropriate, provided that the definition of "any modifications" is narrowed and made relevant to changes with unclear impact on safety or effectiveness, in the context of a small, focused subset of Class II devices. It is not warranted for all Class II devices, or for the "Class IIb" subset proposed by FDA.

The periodic update is not necessary for all Class II devices, (see attached AdvaMed proposal on a small, focused subset of Class II devices, Attachment C), and would impose an unnecessary burden on FDA resources and on industry. It is the responsibility of the 510(k) holder to determine what modifications require a new 510(k) based on regulation and guidance, and FDA currently has a means to evaluate the appropriate reporting of device modifications through the facility inspection program. Changes to a device are routinely reviewed in the course of an FDA inspection of a company's design control procedure and other Quality System Regulation requirements. Revised guidance (K97-1), reflecting FDA's current thinking on device modifications that require a new 510(k), would also aide appropriate decision-making.

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. An "assurance case" is a formal method for demonstrating the validity of a claim by providing a convincing argument together with supporting evidence. It is a way to structure arguments to help ensure that top-level claims are credible and supported. If CDRH pursues this approach, the Center should develop guidance on how submitters should develop and use an assurance case to make adequate, structured, and well-supported predicate comparisons in their 510(k)s. The guidance should include the expectation that all device description and intended use information should be submitted and described in detail in a single section of a 510(k). The 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. CDRH should also develop training for reviewers and managers on how to evaluate assurance cases.*

AdvaMed does not support this recommendation. Adopting the general use of assurance cases is premature and unwarranted. As the Working Group points out in its recommendations, the assurance case framework is not widely used in the medical device industry, either by industry or by FDA. This raises two immediate concerns to industry. First, given that the Working Group 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 to ensure adequate training of existing and new staff. The second concern is that it is not clear what problem is leading FDA to make this recommendation and whether the assurance case is the only or best means of addressing the concern raised by FDA.

The example FDA cited in support of using assurance cases 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 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 assurance cases would be overlooked by FDA reviewers. The FDA has not made the case that they will improve 510(k) submissions for simpler devices. Nor have they made a case for why change is necessary.

Recommendation: *The 510(k) Working Group further 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 allow review staff to develop a better understanding of the device's key features. Currently, CDRH receives photographs or schematics as part of most 510(k)s; however, receiving both as a general matter would provide*

review staff with more thorough information without significant additional burden to submitters. Further, CDRH could include photographs and schematics, to the extent that they do not contain proprietary information, as part of its enhanced public 510(k) database, described below, to allow prospective 510(k) submitters to develop a more accurate understanding of potential predicates. Exceptions could be made for cases in which a photograph or schematic of the device under review will not provide additional useful information, as in the case of software-only devices. 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.

AdvaMed does not support requiring the submission of detailed device photographs or schematics nor does it support the release of detailed photographs and other graphic depictions to the enhanced 510(k) database. 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. Schematics generally provide engineering information (e.g., wiring diagram) that is usually considered proprietary. The same could be said of □detailed□photographs depending on the level of detail required. 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.

AdvaMed recognizes that having a visual image of the device under review may benefit the review process and we support the submission of photographs and drawings of the device (showing the external features) that are necessary to establishing substantial equivalence. 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. In addition, there are some device types, such as software, for which a schematic or photograph is not relevant. Where appropriate, CDRH may ***request*** a photograph or graphic depiction of the device under review as a means to aid the review process and serve as an educational tool, but not state it as a requirement.

AdvaMed does not support *requiring* each 510(k) submitter to keep at least one unit of the device under review available for CDRH to access upon request. Under limited circumstances AdvaMed supports *requesting* submitters to keep one unit of the device available as a sample for CDRH to see during the 510(k) review process with the understanding that the device is used for education of the reviewer, is not appropriate for testing, and that the request does not delay the review of the submission. AdvaMed recommends that the request be made only when seeing the actual device is necessary for determining substantial equivalence, with FDA developing criteria and sharing them with the industry for when such a request for a device is appropriate. When a request is made, CDRH must consider the logistics related to such a request. Delivering large pieces of equipment to FDA facilities makes little sense. Large pieces of equipment will require loading dock/receiving areas as well as secure storage within an appropriate storage

environment. At any one time, CDRH could have thousands of devices requiring storage at the White Oak facility. If CDRH expects equipment to be operational, it may require special installation and calibration activities. It is also important to be mindful that in some cases it would be necessary for the reviewer to examine the device at the manufacturing facility because of device size or installation requirements. 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.

In addition, keeping a device available indefinitely so it can be examined when it is cited as a predicate is impractical for industry 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, with no commensurate benefit to public health. 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.

CDRH also must recognize that a device sample submitted during 510(k) review might not be a product of the standard manufacturing process, but may be a manufacturing equivalent prototype or functional model. As noted, in some cases, the device in its final form may not exist at the time of 510(k) submission. In some cases, manufacturers may not be "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, AdvaMed recommends that the availability of a sample device during the review be a CDRH *request* and not a requirement.

Improper Recognition of Standards

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."*

AdvaMed strongly supports the recommendations 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).

Numerous domestic and international consensus standards address aspects of safety and/or effectiveness relevant to medical devices, and many of these standards have been developed with the participation of CDRH staff. A person required to submit a 510(k) must provide information as required by the statute and regulations to allow CDRH to make an appropriate decision regarding clearance of the device. Conformance with recognized consensus standards plays an important part in satisfying some or all of these premarket review requirements.

Current guidance[9] states "CDRH believes that conformance with recognized consensus standards can support a reasonable assurance of safety and/or effectiveness for many applicable aspects of medical devices." For 510(k)s, information on conformance with recognized consensus standards helps to establish the substantial equivalence of a new device to a legally marketed predicate device. This information may be used to show that the new device is as safe and effective as the predicate in the areas covered by the standards. Moreover, if any premarket submission includes a declaration of conformity to recognized consensus standards that contain pass/fail criteria, this declaration should, in most cases, minimize the need for CDRH to review the actual test data for those aspects of the device addressed by the standards.

Existing FDA guidance on "Recognition and Use of Consensus Standards"[10] also 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:

- Conformance to a standard may not address all safety and efficacy questions about a device
- Only certain aspects of the standard may be recognized by FDA
- What documentation is needed regarding the appropriate use of standards, and any deviations from the standard
- Appropriate use of "declarations of conformity," with inclusion of the testing results, if the standard does not include pass/fail criteria

AdvaMed does not support revising the requirements for "declaration of conformity by requiring submitters to provide a summary of testing to demonstrate conformity. The guidance clearly notes that falsifying a declaration of conformity is a prohibited act under Section 301(x) of the Act. Therefore, requiring all submitters to provide a summary of testing to demonstrate conformity, even when the standard contains pass/fail criteria, is unnecessary, and would undermine the basic tenet of the Abbreviated 510(k) process, which is another important and valuable part of the 510(k) program.[11]

With the increased move toward globalization, AdvaMed urges FDA to continue to be involved in the standards development process and to formally recognize consensus standards early and to the fullest extent possible. We also strongly support the recommendations that CDRH provide additional guidance and training for industry and review staff regarding the appropriate use of those consensus standards, including proper documentation within the 510(k). We encourage CDRH to provide more concise examples of how manufacturers may be inappropriately using the standards, and how they might use them more effectively.

Incomplete Information

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9 Guidance for Industry and FDA Staff Recognition and Use of Consensus Standards. September 17, 2007.

10 Ibid.

11 See Section 514

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.*

AdvaMed does not support this recommendation for all submitters to provide this information. 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. Applying this requirement automatically to all Class II devices and those Class I devices on the reserve list is excessive and suggestive of current PMA requirements (potentially eroding the distinctions between 510(k) and PMA).

AdvaMed is concerned that the Working Group proposal requests not only information that the 510(k) sponsor knows, but also all scientific information regarding the safety and/or effectiveness that should be reasonably known to the sponsor. This reflects the PMA standard for information on safety and effectiveness, not the 510(k) standard for showing substantial equivalence. This standard departs from the substantial equivalence determination established by law in Section 513(i) of the Act by implying that a full review of safety and effectiveness would be required. In addition, the language is too vague for industry to provide a consistent set of information to CDRH in any given 510(k) filing. Without a clear and reasonable definition of CDRH expectations, the 510(k) sponsor would not know whether they have met the requirement until they receive feedback under the 510(k) process from CDRH. The 510(k) sponsor also would be limited in the amount of information available for a predicate device that was not their own design.

In addition, 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. As discussed elsewhere within these comments, Least Burdensome requirements do apply to 510(k) submissions and should be applied to this specific recommendation.

The example CDRH provides in its report for 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). Requiring submission of all scientific information for all 510(k)s is an excessive remedy that is poorly tailored to the example proffered. In fact, this example is adequately covered by the Truthful and Accurate Statement that companies are required to sign with each 510(k) submission. Most companies understand well 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) accurately represents the safety and effectiveness of the new device. One must assume that, in an extreme 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.

A final consideration for CDRH is whether a requirement for all scientific information could be implemented without statutory change. AdvaMed recognizes that FDA may request any information regarding safety and effectiveness about a device under review when that information is necessary to make the substantial equivalence determination (21C.F.R. § 807.87(1). However, it is not clear whether, *a priori*, 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 meets this test and is necessary to the substantial equivalence determination of all 510(k)s. Therefore, AdvaMed believes that implementation of this as a pre-stated requirement for all devices would require a statutory change.

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.*

AdvaMed does not support the recommendation to identify a subset of Class II devices called "Class IIb." While AdvaMed supports strengthening the 510(k) process by providing enhanced transparency and predictability to the CDRH reviewer expectations for a small, focused subset of Class II devices, 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.[12] AdvaMed submitted its own proposal for a small focused subset of Class II devices to the docket (see Attachment C). We would like to re-emphasize that our proposal was not meant to, nor do we expect it will, create a new classification scheme for medical devices in the United States, but rather creates an informal, small, focused subset of Class II device types for which CDRH has provided advanced notice that additional information beyond that normally provided in a 510(k) may be expected to support a substantial equivalence determination. It is important to note that the AdvaMed proposal provided suggestions for a number of additional submission requirements that could be required for a device in the subset; it did not recommend that all devices in the subset be required to comply with all enhanced requirements. Nor did it suggest that all devices for which CDRH currently requires clinical information automatically become members of the subset.

Therefore, as this proposal is further developed, we urge CDRH to focus the AdvaMed's proposal for 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

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

submissions for certain 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.

AdvaMed believes that its proposed special controls for a small subset of Class II devices provides an opportunity to consider the down-classification of certain Class III devices with a proven track record of safety and effectiveness. The special controls would allow the Agency to establish any additional pre- and postmarket requirements that may be deemed necessary for such down-classified devices.

For any subset of Class II devices, it is necessary to define clear criteria and standards that apply, through a public notice and comment period, for determining which device types fall within this higher risk subset. The types of devices that would fall into this subset would be determined based on risk management processes, and could include certain permanent implants, 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. However, permanent implants, life-sustaining devices, and life-supporting devices with a record of safety in clinical use or with up-to-date standards, guidance and/or special controls that have proven effective would **not** warrant placement in the higher risk subset.

We disagree with OIVD's recent public comment that all Class II *in vitro* diagnostic devices for which clinical data are required should be in the higher risk subset of Class II.[13] While the regulations at 21 C.F.R. §809.10 provide for performance data, CDRH interprets this, in many cases, to mean clinical data comparing IVD performance to whatever OIVD determines to be the "gold standard." There is little evidence to suggest that the current 510(k) contents fail to provide sufficient information to enable OIVD to clear safe and effective devices. If, in fact, any IVDs are to be a part of this subgroup, the decision should be risk based, consistent with the principles of AdvaMed's *Risk-Based Approach for the Regulation of All Diagnostics*, and be supported by evidence of significant issues with an entire category of products.

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."*

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[13] See transcript of August 31, 2010 CDRH webinar on the CDRH 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.

AdvaMed does not support the recommendation to create a Class IIa and a Class IIb. AdvaMed agrees that training for review staff and industry is essential in providing safe and effective products to patients, however we disagree with the name and the concept of Class IIa and Class IIb. The names imply a new classification structure that exceeds the current statutory authority of the Agency. If a guidance for a small Class II subset of devices is developed, it must be made clear to both the review staff and industry that this is not considered device reclassification or creation of a new classification scheme. Once the criteria and process for a "small subset of Class II" is developed and is subject to notice and comment, AdvaMed encourages training of review staff and industry on the application and implementation of relevant guidances.

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.*

AdvaMed does not agree with FDA's premise of a Class IIb designation. AdvaMed agrees that CDRH should provide greater clarity regarding the circumstances in which it will request clinical information in support of a 510(k), and what type and level of clinical information is adequate to support clearance. Although not explicitly identified by the 510(k) Working Group as an issue, AdvaMed believes that greater clarity is needed in distinguishing clinical information intended to support 510(k) clearance from clinical information supporting PMAs.

Examples of clinical information that may be used to support substantial equivalence may consist of published and/or unpublished reports on other clinical experience of either the device in question or a justifiably comparable device, results of pre-and postmarket clinical investigation(s) or other studies reported in the scientific literature of a justifiably comparable device, or results of pre- and postmarket investigation(s) of the device.

As part of the larger regulatory picture, the 510(k) submission process assures safety and effectiveness by demonstrating substantial equivalence and documenting critical aspects of device performance and mitigating risks. If Congress intended for the 510(k) process to assure safety and effectiveness in absolute terms (rather than through a comparative lens), then both the regulatory and resource requirements under this section of the Act would need to change as would resources to accompany such expectations. CDRH should keep in mind that most devices

have a long history of safe and effective use that precludes the need for clinical data or clinical evidence.

In the context of a "subset of Class II" submission, AdvaMed supports this recommendation for those devices in the subset that require clinical information to establish substantial equivalence. However, AdvaMed does not support the concept that all IVD devices for which the Office of In Vitro Diagnostics has historically requested clinical data, should be placed in the subset of Class II devices. For many IVD devices, performance information, as specified in 21 C.F.R. §809.10, is sufficient to establish substantial equivalence. The requirement for clinical data should only apply to those IVD devices that require clinical data to establish substantial equivalence because there is no acceptable comparator or because the test or technology is new and it is not possible to tie the results to a clinical condition or diagnosis.

AdvaMed supports the recommendation that CDRH define the term "clinical data." AdvaMed recommends that CDRH review the definitions for "clinical evidence", "clinical data" and "clinical evaluation" provided in the GHTF document "Clinical Evidence-Key Definitions and Concepts" (SG5/NIR8:2007). Harmonization with these definitions would foster a common understanding among not only CDRH review staff and industry but also with international regulatory agencies

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.*

AdvaMed does not support this 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 require postmarket studies as part of premarket special controls and through Section 522 postmarket surveillance orders, further authority is unnecessary and may lead to a proliferation of burdensome postmarket studies that add little to enhance public health.

AdvaMed supports the recommendation with modifications to explore greater use of CDRH's existing postmarket authorities for a subset of Class II devices. Under existing authorities, FDA can issue orders for post-market data through Section 522 of the Act, and in the case of special controls, under Section 513(a)(1)(B) of the Act, can require postmarket data through performance standards, postmarket surveillance, and patient registries.

Recommendation: *The 510(k) Working Group further recommends that CDRH 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 premarket submission for future 510(k)s.

AdvaMed supports UDI for medical device labels based on the option of following GS1 or HIBCC standards implemented in a risk-based manner with an appropriate implementation timeframe. We look forward to receiving a more detailed proposal in the form of a proposed rule subject to public notice and comment. It should be noted that submitters of 510(k)s may have limited or no access to device databases and electronic health record systems. We do not support exploring how data collected or associated with UDI may be used as part of the 510(k) process, as it is premature at this time, and recommend CDRH defer evaluation of this option until such time as UDI is effective.

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.*

AdvaMed supports this recommendation for only a small number of specific device types within the subset of Class II devices for which particular circumstances or conditions would require the submission of a summary of manufacturing information (e.g., manufacturing includes a unique process that is critical to the safety or efficacy of the device). Further, rather than submitting the level of detail required for PMA submissions, CDRH should clarify via guidance that only a summary (e.g., flow chart) of the manufacturing information relevant to safety and effectiveness of a device is required.

AdvaMed does not support manufacturing information being provided for any *in vitro* diagnostic device in Class II. Although in its report, CDRH indicates this requirement is appropriate for any product with lot-to-lot variability, it typically is not the manufacturing process that introduces variability.

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.*

AdvaMed supports the recommendation to clarify when it is appropriate for CDRH to use its current authority.

There would be no benefit to the public health from withholding substantial equivalence determinations for a subset of Class II devices, or any devices, because of alleged failures to comply with good manufacturing practice requirements (GMPs) unless there is a substantial

likelihood that the failure to comply with GMPs will potentially present a serious risk to human health. Section 513(f)(5) in FDAMA was enacted in response to FDA's extra-legal creation and use of the "reference list," to withhold 510(k) clearances until FDA verified that alleged GMP violations identified in inspections were corrected. In response to this program, Congress was "concern[ed] that FDA was inappropriately using the device premarket notification process for compliance purposes."[14] "This process was unfair and denied device manufacturers an opportunity to dispute effectively FDA's allegations that firms were not in GMP compliance. FDA set itself up as judge and jury and, in essence, administratively enjoined the classification of devices . . . ."[15]

The reference list unjustifiably delayed 510(k) clearances until alleged GMP violations were remedied and the Agency re-inspected the facility to confirm remediation. This led to significant delays in substantial equivalence determinations, resulting in physicians and patients being denied the availability of new devices.[16] More importantly, GMP corrections had nothing to do with a determination of substantial equivalence (classification of a medical device). Simply put, devices were withheld from the public, in most instances, without any actual health justification.

In eliminating the reference list, Congress maintained a link between GMPs and 510(k) by permitting the withholding of substantial equivalence determinations where a non-compliance presented "a substantial likelihood that the failure to comply with [GMPs] will potentially present a serious risk to human health."[17] In other words, Congress believed that more harm would be done to the public health by withholding the initial classifications of devices than letting them go forward, unless a significant health harm related to a GMP violation was likely.

The Agency is vested with substantial enforcement authorities to ensure compliance with its laws and can prohibit the distribution of adulterated or misbranded devices. To force enforcement considerations into the premarket context would delay the entire premarket review process without a net benefit to the public. The 510(k) process is one of classification and comparison to a legally marketed device. It is not an evaluation of whether a company is in compliance with the Act, nor should it be. Indeed, the legislative history of Section 513(f)(5) states that "[c]learly, FDA has substantial authority to enforce the Act against illegal devices and the persons who market them. It is unacceptable that the Agency misuse premarket notification to avoid enforcing the Act."[18]

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14 Senate Report No. 105-43, 105th Cong. 1st Sess., at 29.

15 *Id.*

16 *See id.* (stating, "[o]ver the past five years, the FDA has withheld device classification determinations of substantial equivalence because of its belief that firms were not in compliance with good manufacturing practices.").

17 *See* "513(f)(5).

18 *Id.*

A substantial equivalence determination does not void or otherwise limit FDA exercise of its enforcement authorities under the Act nor does it empower recipients of substantial equivalence orders to introduce into commerce misbranded or adulterated devices. Congress explained that:

> FDA can find a device substantially equivalent to a predicate device and still inform the device manufacturer that . . . it should not be marketed because of the Agency's view that the device does not comply with the law in some specified respect. Then, if a person markets the device after such notice, FDA can enforce the Act.[19]

The Act describes a complete regulatory regime that includes premarket review processes and substantial authority to remove violative devices from the market, especially including those that present potential harm to the public health. Congress was fully aware of the immense authority it vested in the FDA to maintain the Congressional balance of not over-regulating devices in the premarket context, while ensuring that only safe and effective devices can be introduced into commercial distribution.

AdvaMed recommends that if the Agency determines that a substantial equivalence determination should be withheld because a GMP non-compliance presents "a substantial likelihood that the failure to comply with [GMPs] will potentially present a serious risk to human health," the target company be afforded the due process opportunity to discuss the decision with the Agency prior to the Agency taking action.

AdvaMed does not support pre-clearance inspections for the device types in the subset of Class II devices or any 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.

Recommendation: *CDRH should take steps to enhance its internal and public information systems and databases to provide easier access to more complete information about 510(k) devices and previous clearance decisions.*

Product Codes

Recommendation: *The 510(k) Working Group recommends that CDRH develop guidance and Standard Operating Procedures (SOPs) on 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.*

AdvaMed supports this recommendation. AdvaMed also recommends that CDRH include a process for alerting the public (industry) when new product codes are established.

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19 *Id.*

Recommendation: *510(k) Working Group further recommends that CDRH enhance existing staff training on the development and assignment of product codes.*

AdvaMed supports enhanced staff training on the development and assignment of product codes.

510(k) Databases

Limited Tools for Review Staff and Outside Parties

Recommendation: *The 510(k) Working Group recommends that CDRH develop a publicly available, easily searchable database that includes, for each cleared device, a verified 510(k) summary, photographs and schematics of the device, to the extent that they do not contain proprietary information, 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.*

AdvaMed agrees that CDRH should develop an easily searchable database that provides appropriate information to the public. AdvaMed agrees that the database should include a verified 510(k) summary. 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. AdvaMed agrees with CDRH comments that publicly 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. The decision summaries currently posted by the OIVD for IVD clearances have proven to be a valuable tool to industry. The decision summary, in combination with consistent, verified 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 510(k) 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.

It should be noted that AdvaMed recommends eliminating the option for submitters to provide a 510(k) Statement in lieu of a 510(k) summary. This change will assure that consistent and high quality information about any new or modified 510(k) device will be readily available to the public.

AdvaMed does not, however, support the posting of photographs, schematics, and other graphic depictions of devices on the searchable database. Schematics are proprietary information and should not be posted in a publicly-searchable database. Further, photographs and other depictions submitted with the 510(k) for the purpose of establishing substantial equivalence and educating the reviewer may be cosmetically different than the marketed device, thereby causing confusion for the public. Foreign competitors may use this information to produce counterfeit

devices or to shorten device development times and speed their time to market, resulting in competitive harm to U.S. companies. Competitive advantages afforded to foreign and domestic competitors would exist even when actual proprietary information is not disclosed.

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.*

AdvaMed supports CDRH's development of 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 with the requirements. We also recommended that FDA consider providing a template, to assure that the quality of information in 510(k) Summaries is consistent and complete. This template will provide information that 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. AdvaMed is developing a standardized format and template for 510(k) summaries, which we will be pleased to provide to CDRH for its consideration and use.

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. In exploring this approach, CDRH should consider options to assure that labeling could be screened efficiently, without placing a significant additional burden on review staff. For example, to allow for more rapid review of labeling changes, the Center could consider the feasibility of requiring manufacturers to submit a clean copy and a redlined copy of final labeling and subsequent updates, highlighting any revisions made since the previous iteration. As a longer-term effort, the Center could explore greater use of software tools to facilitate rapid screening of labeling changes. 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.*

AdvaMed does not support this recommendation. AdvaMed believes that the Working Group's assumption of benefits to medical professionals and device users are overstated. Collection, organization, editorial checks of redlined copy, and posting in a database by CDRH review staff will require a significant investment of resources (both human and technological) without meaningful benefit to the public health. Labeling of some devices contains information that is intended for hospitals or practitioners. Public misuse or confusion may result, if such labeling is broadly available to the public (such as how to program some electrical devices). Public posting of preliminary labeling would provide undue benefit to competitors and would inhibit U.S. innovation. AdvaMed 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. When it is determined appropriate by a manufacturer, labeling information is provided on a manufacturer's website and is controlled by the manufacturer to maintain accurate up-to-date labeling, and if necessary, lot-specific labeling (e.g., certain IVD products).

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.*

AdvaMed supports this recommendation 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 U.S.-registered foreign devices. It also would be valuable for CDRH to show the full chain of 510(k) ownership.

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.*

Reviewer Expertise and Experience

Recommendation: *The 510(k) Working Group recommends that CDRH continue to take steps to enhance recruitment, retention, training, and professional development of review staff, including*

providing opportunities for staff to stay abreast of recent scientific developments and new technologies. This should include increased engagement with outside experts, as discussed further in the preliminary report of the Task Force on the Utilization of Science in Regulatory Decision Making (described further in Section 2, below).

AdvaMed supports this recommendation. AdvaMed agrees that CDRH should continue efforts to enhance recruitment, retention, training, and development of review staff. AdvaMed agrees with the approach noted multiple times in the recommendations that proper development and delivery of appropriate training is key to the success of any organization and to successful implementation of any change. We also agree that well-designed and effectively delivered training will lead to the greatest likelihood of program success and should be directed at both CDRH staff and industry.

In addition, AdvaMed offers the following suggestions as FDA explores opportunities to enhance its training program. We believe that the "train the trainer" approach works 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. The use of outside experts and a "train the trainer" approach will minimize the amount of CDRH managers' time needed to perform the number of training sessions that will be required to accomplish these changes.

AdvaMed recommends that staff training require testing or proof of proficiency, similar to the requirements for training industry personnel described in Quality System Regulation. We also believe that this training should be required before staff is empowered to perform reviews or assessments under any new procedures. This training would parallel 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: *The 510(k) Working Group further recommends that CDRH consider establishing a Center Science Council comprised of experienced reviewers and managers and under the direction of the Deputy Center Director for Science. The Science Council should serve as a cross-cutting oversight body that can facilitate knowledge-sharing across review branches, divisions, and offices, consistent with CDRH's other ongoing efforts to improve internal communication and integration. The Science Council's role in improving the consistency of Center decisions is discussed in greater detail in the preliminary report of the Task Force on the Utilization of Science in Regulatory Decision Making.*

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AdvaMed supports the establishment of a Center Science Council comprising experienced employees and managers under the direction of the Deputy Center Director for Science to provide oversight and help assure consistency across the Center.

The process and activity of the Council must be transparent to all stakeholders. Roles should be clearly defined for this group and made publicly available.

To enhance the value the Council can provide, the Agency should ensure that the Council provides oversight to assure consistency and integrity of the 510(k) process, rather than engaging in routine decisions that may have the unfortunate effect of undermining the process. Further, the Council should not have the authority to reverse decisions.

This process for managing new scientific information **should not be used to reach recommendations applicable to individual devices without input from the entity with legal authority to market the device**. It should not replace any legally required processes such as the current consultative and appeals routes, or otherwise render these processes superfluous to substantive outcomes. The Center Science Council should be trained to understand FDA's legal authorities and processes, in order to assure that the Council focuses appropriately on "regulatory science" rather than "pure science" in providing Center oversight.

Third Party Review

Recommendation: *The 510(k) Working Group recommends that CDRH develop a process for regularly evaluating the list of device types eligible for third-party review and adding or removing device types as appropriate based on available information. The Center should consider, for example, limiting eligibility to those device types for which device-specific guidance exists, or making ineligible selected device types with a history of design-related problems.*

AdvaMed does not support the recommendation to limit eligibility for Third Party review as stated. As noted in CDRH's 510(k) Working Group Preliminary Report and Recommendations, Third Party Reviews were established under FDAMA. Medical devices are eligible for Third Party Review except as prohibited in Section 523(a)(3) of the Act, where it states, "An Accredited person may not be used to perform a review of "(i) a Class III device; (ii) a Class II device which is intended to be permanently implantable or life sustaining or life supporting; or (iii) a Class II device which required clinical data in the report submitted under Section 510(k) for the device." The current law has no other eligibility requirements, such as device-specific guidance documents, or other imposed criteria.

The purpose of the Accredited Persons Program (AKA Third Party Review) is to implement Section 523 of the Act by accrediting third parties to conduct the initial review of 510(k)s for selected low-to-moderate risk devices. The Accredited Persons Program was intended to enable FDA to use its scientific review resources for higher-risk devices, while maintaining a high degree of confidence in the review of low-to-moderate risk devices by Accredited Persons, and

to provide manufacturers of eligible devices an alternative review process that may yield more rapid 510(k) decisions.

Recommendation: *The 510(k) Working Group further recommends CDRH enhance its third-party reviewer training program and consider options for sharing more information about previous decisions with third-party reviewers, in order to assure greater consistency between in-house and third-party reviews.*

AdvaMed supports this recommendation. AdvaMed supports CDRH enhancing its third-party reviewer training program; we also recommend periodic retraining and auditing of third party reviewers.

While the 510(k) Report referenced quality issues with the Third Party Review program, it is important to note that the report cited an analysis of third party reviews during the last 9 months of 2005, a very small and potentially outdated sample of the program as it exists today.

Seven percent of 510(k)s, or in excess of one thousand 510(k)s submitted to CDRH over the last 5 years were reviewed by Third Parties, illustrating that the program remains important to both industry and the Agency, and that it should be preserved and improved as necessary. The Accredited Persons program provides a pool of trained and qualified resources, assisting the Agency in the review of 510(k)s, and in some ways, acting in the capacity of the Ad Hoc review team as noted within the 510(k) Report.

The medical device industry values the Third Party review process as described in the law, and as currently implemented by CDRH. As requested by Dr. Shuren in the Forward of the 510(k) report, AdvaMed recommends the following potential alternatives for improving the program rather than reducing the devices eligible for Third Party Review:

- The 510(k) report states, Concerns have also been raised about the level of training and experience of accredited third parties. CDRH offers training for third-party reviewers, but it is only offered every 3-4 years. FDA assessment, accreditation, and training of Accredited Persons should occur not only upon acceptance of an Accredited Party into the program, but on an ongoing, periodic basis, thereby ensuring continued qualification of the Third Party review organizations.

- FDA should periodically audit the personnel qualifications for Accredited Persons, to ensure they are equivalent to the level within the CDRH s Office of Device Evaluation.

- FDA should periodically audit each Accredited Person to ensure performance and to inspect records, correspondence, and other materials relating to Accredited Person to ensure the quality of the reviews.

- In accordance with Section 523(b)(2) of the Act, FDA may suspend or withdraw accreditation from a Third Party, after providing notice and an opportunity for an informal hearing, when a Third Party:
  1) is not substantially in compliance with Section 523;
  2) fails to act in a manner consistent with the purposes of Section 523; or
  3) poses a threat to public health.

- FDA should educate and enforce the requirement that it is a prohibited act under Section 301(y)(1) for an Accredited Person, to:

  1) submit a report that is false or misleading;
  2) disclose confidential information or trade secrets without the submitter's consent; or
  3) receive bribes or perform a corrupt act.

- The 510(k) Working Group notes that Third Parties lack access to predicate information and to new postmarket safety information, and they find it challenging to keep up with CDRH's evolving evidentiary expectation in the absence of device specific guidance. Prior to initiating a 510(k) review, the Accredited Person should contact the appropriate CDRH Office of Device Evaluation (ODE) Branch Chief (or designee) to identify pertinent issues and review criteria, obtain non-confidential predicate information such as the reviewers' decision summary for the predicate device(s), and discuss any new postmarket safety information related to this type of device. In this way, the Accredited Person will be able to stay abreast of CDRH's evolving evidentiary expectations. Posting of 510(k) summaries on a public database also will assist in keeping Accredited Persons current on evidentiary expectations.

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

Recommendation: *The 510(k) Working Group recommends that CDRH 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.*

AdvaMed 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.

Each metric should be focused on a specific question or aspect of the program. Collectively and individually, the metrics need to be simple and unambiguous both to FDA staff and to other

stakeholders. The metrics 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 or more 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.

Recommendation: *The 510(k) Working Group further recommends that CDRH periodically audit 510(k) review decisions to assess adequacy, accuracy, and consistency. The ongoing implementation of iReview (described in Section 5.3.2 of this 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.*

AdvaMed is encouraged by CDRH's intent to assess the effectiveness of the review process, and to drive greater knowledge and consistency among reviewers. These periodic audits of review decisions should not be punitive and should be for the purpose of assessing the review process and ensuring consistency across the Agency, not putting the Science Council in the position of reversing earlier decisions. For that reason, if CDRH moves forward with such audits, it will be critical for CDRH to clearly define objective audit criteria and the authority of the Council and to share those criteria with staff and industry. CDRH and industry need to have the same understanding of expectations for the 510(k) program to be effective. In addition, if CDRH conducts such audits, any major lessons learned should be communicated to the industry in a timely manner, with sufficient transition time to ensure that any changes in expectations during a pending submission do not result in significant delays.

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VOLUME II-UTILIZATION OF SCIENCE IN REGULATORY DECISION MAKING

General Comments

As a science-based agency, FDA is charged with basing its decisions on valid scientific information. However, information is not science simply because it is used in decision making. Science involves the testing of hypotheses and the repeatability of experiments, not simply the collection of unverified information. While some anecdotal or new information may be true and useful, much of it will not meet standard criteria for science and may require confirmatory studies.

Specific Comments

1. Enhancing CDRH's Scientific Knowledge Base

Recommendation: *CDRH should take steps to improve its ability to readily access high-quality information about regulated products.*

Premarket Review

Interpretation of the "Least Burdensome" Provisions

Recommendation: *The Task Force recommends that CDRH revise its 2002 "least burdensome" guidance to clarify the Center's interpretation of the "least burdensome" provisions of the Federal Food, Drug, and Cosmetic Act (21 USC § 360c(a)(3)(D)(ii) and 21 USC §360c(i)(1)(D)). CDRH should clearly and consistently communicate that, while the "least burdensome provisions" are, appropriately, meant to eliminate unjustified burdens on industry, such as limiting premarket information requests to those that are necessary to demonstrate reasonable assurance of safety and effectiveness or substantial equivalence, they are not intended to excuse industry from pertinent regulatory obligations nor to lower the Agency's expectations with respect to what is necessary to demonstrate that a device meets the relevant statutory standard.*

AdvaMed does not support the recommendation to revise the current Least Burdensome guidance document. The Report (page 17) notes that the staff at FDA are concerned about their ability to require companies to submit additional data in their 510(k)s when those data have not traditionally been required for similar products. The fact that companies raise the least burdensome requirement of the law as a defense against complying with such requests or as a basis for complaints to the Ombudsman does not mean that the section of the law or the guidance developed in 2002 by CDRH are inadequate. AdvaMed agrees with the FDA s characterization of this provision that the ..goal was to streamline the regulatory process (i.e., reduce burden) to improve patient access to breakthrough technologies not lower the statutory criteria for determination of substantial equivalence.

The provisions of the Act are clear:

Section 513(a)(3)(D)(ii)
"Any clinical data, including one or more well-controlled investigations, specified in writing by the Secretary for demonstrating a reasonable assurance of device effectiveness shall be specified as a result of a determination by the Secretary that such data are necessary to establish device effectiveness. The Secretary shall consider, in consultation with the applicant, the least burdensome appropriate means of evaluating device effectiveness that would have a reasonable likelihood of resulting in approval."

Section 513(i)(1)(D)
"Whenever the Secretary requests information to demonstrate that devices with differing technological characteristics are substantially equivalent, the Secretary shall only request information that is necessary to making substantial equivalence determinations. In making such requests, the Secretary shall consider the least burdensome means of demonstrating substantial equivalence and request information accordingly."

It appears that the principal issue is the need for education and training of industry and CDRH staff to improve their understanding of the meaning and intent of the least burdensome provision.

Education and training of industry and staff of the least burdensome principles are appropriate steps. As noted in the report, the background of FDA "least burdensome guidance states, "[i]n order for the least burdensome approach to be successful, it is important that industry continue to meet all of its statutory and regulatory obligations, including preparation of appropriate scientifically sound data to support applications." The report further notes, "[t]hese principles are consistent with good governance in general." Rather than begin with revision of the guidance, we recommend the Agency concentrate its efforts on education and training of industry and staff on the principles of least burdensome. The guidance document issued in October of 2002 implemented provisions of FDAMA 1997 approximately five years after its enactment. It was issued as a draft subject to notice and comment, and then re-issued as a final guidance after consideration of the comments received. Continued education and training are a necessary step to ensure adequate understanding and application of the least burdensome principles and should be implemented and evaluated prior to any revision of this guidance.

FDA should communicate clearly and consistently that the least burdensome provision is meant to eliminate unjustified burdens on industry. The Agency also should emphasize that the provisions are not intended to lower the Agency's expectations with respect to what is necessary to demonstrate that a device meets the relevant statutory standard.

"Least Burdensome" is a valuable concept for not only FDA processes, but for all government regulation. In fact, the current administration has recently issued a request to all agencies asking them to work in a least burdensome fashion. Executive Order 12866 directs agencies "to foster the development of effective, innovative, and least burdensome regulations" (Section 6(a)(2)), and to "identify and assess available alternatives to direct regulation, including . . . providing

information upon which choices can be made by the public (Section 1(b)(3)). Executive Order 12866 also directs agencies to analyze potentially effective and reasonably feasible alternatives to the planned regulation, identified by the agencies or the public (including improving the current regulation and reasonably viable nonregulatory actions) (Section 6(a)(3)(C)(iii)).

Quality of Clinical Data

Recommendation: *The Task Force recommends 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), in part by developing guidance on the design of clinical trials that support PMAs and establishing an internal team of clinical trial experts who can provide support and advice to other CDRH staff, as well as to prospective investigational device exemption (IDE) applicants as they design their clinical trials. The Center should work to assure that this team is comprised of individuals with optimal expertise to address the various aspects of clinical trial design, such as expertise in biostatistics or particular medical specialty areas. The team would be a subset of the Center Science Council discussed in Section 4.2.1 of this report, and, as such, it may also serve in the capacity of a review board when there are differences of opinion about appropriate clinical trial design and help assure proper application of the least burdensome principle. CDRH should also continue to engage in the development of domestic and international consensus standards, which, when recognized by FDA, could help establish basic guidelines for clinical trial design, performance, and reporting. In addition, CDRH should consider expanding its ongoing efforts related to clinical trials that support PMAs, to include clinical trials that support 510(k)s.*

AdvaMed supports the development of guidance on the design of clinical trials for support of PMAs and, when necessary, 510(k)s. This guidance should address the wide range of clinical trial designs and not be limited only to randomized controlled trials. AdvaMed strongly recommends that CDRH include industry in the guidance development process thus allowing valuable input from experienced and knowledgeable industry clinical staff.

AdvaMed supports CDRH's establishment of an internal team of clinical trial experts who can provide support and advice to FDA staff as well as prospective investigational device exemption (IDE) applicants.

AdvaMed also strongly supports CDRH's involvement with the development of domestic and international consensus standards that would be recognized by FDA and provide harmonization of requirements.

Recommendation: *The Task Force recommends that CDRH work to better characterize the root causes of existing challenges and trends in IDE decision making, including evaluating the quality of its pre-submission interactions with industry and taking steps to enhance these interactions as necessary. For example, the Center should assess whether there are particular types of IDEs that tend to be associated with specific challenges, and identify ways to mitigate those challenges. As part of this process, CDRH should consider developing guidance on pre-*

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submission interactions between industry and Center staff to supplement available guidance on pre-IDE meetings.

AdvaMed supports this recommendation. AdvaMed supports efforts to improve the IDE decision making process including the evaluation and possible enhancement of interactions with industry. AdvaMed has previously submitted to FDA (April 18, 2009) an analysis of existing pre-submission meetings and recommendations for best practices as it relates to these meetings for the life-cycle of product development and approval. AdvaMed would welcome an opportunity to work with CDRH to maximize the efficiency and quality of the IDE review and decision making process.

Review Workload

Recommendation: *The Task Force recommends that 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. The Center's staffing needs are discussed further below.*

AdvaMed is pleased that FDA is addressing its capacity to respond to surges in review workload in a standardized way. CDRH has in the past drawn on knowledge and expertise from across the Center to address time-critical work or work that required a specific expertise that resided in select individuals. The process, however, was not consistent. Having a more formal process to address such needs will make the review process more predictable across review divisions. This would be particularly useful when there are potentially competing needs from different review groups.

There are four recommendations that we would like to make as this process is developed. The first is that the Agency develops a method to assure the appropriate needs and skills are identified up front. As noted in the report, this is necessary to assure that the work being requested of an *ad hoc* team is within their skill set. It is important to ensure that members of the team are adequately trained and have sufficient knowledge of the technologies and issues related to the particular devices being reviewed. The second recommendation is that the *ad hoc* team includes at least one member from the relevant reviewing branch. The third recommendation is that there is a mechanism for oversight of the work of such teams separate from the proposed review of routine reviews. We believe this is necessary to assure the consistency of review work within branches no matter who is performing the reviews and to provide a mechanism to evaluate the impact of the broader and more formal program in this arena. Lastly, we believe it is important that the creation of an *ad hoc* team to address time-critical work does not adversely

affect routine review work, especially in the review divisions from which the members of the *ad hoc* review team were selected.

Recommendation: *The Task Force recommends that CDRH assess and better characterize the major sources of challenge for Center staff in reviewing IDEs within the mandatory 30-day timeframe, and work to develop ways to mitigate identified challenges under the Center's existing authorities.*

AdvaMed believes that expending valuable Center resources to evaluate the sources of challenge for Center staff in complying with the mandatory 30-day timeframe is unnecessary. We believe that with appropriate guidance for pre-IDE meetings and with well-managed and productive pre-IDE meetings, Center staff will accommodate the 30-day timeframe. AdvaMed would welcome an opportunity to work with the Center to mitigate the challenges and increase process efficiency and quality.

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.*

AdvaMed supports efforts to develop additional data sources. However, continued validation of data owners, research contractors, study methods, and data sets are necessary. Criteria for the selection of data sources should be established. Data owners, research contractors, study methodologies, and data sets should be evaluated and validated for accuracy, relevancy and quality. With respect to relevance, it will be important to validate in advance which data sets are capable of answering which types of queries to ensure that inappropriate queries are not sent to data owners which could potentially result in invalid responses. There should be a periodic auditing process to ensure the continued validity of the methodologies and data sets.

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*

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Center's ongoing efforts under its FY 2010 Strategic Priorities to enhance the recruitment, retention, and development of high-quality employees.

AdvaMed supports this recommendation. AdvaMed encourages CDRH to determine essential functions that support the FDA priorities of protecting public health and access to improved medical treatment and focus resources on these functions. Recruitment and training and professional development of highly qualified and motivated employees are essential to achieve CDRH goals. AdvaMed supports CDRH making greater use of site visits, including industry site visits.

Recommendation: *The Task Force recommends that CDRH continue the integration and knowledge management efforts that are currently underway as part of the Center's FY 2010 Strategic Priorities. As part of these efforts, the Task Force recommends that CDRH develop more effective mechanisms for cataloguing the Center's internal expertise, assess the effectiveness of the inter-Office/Center consult process, and enhance the infrastructure and tools used to provide meaningful, up-to-date information about a given device or group of devices to Center staff in a readily comprehensible format, to efficiently and effectively support their day-to-day work.*

AdvaMed supports this recommendation. It is essential that CDRH have the tools and infrastructure necessary to allow reviewers to access relevant internal expertise and have meaningful, up-to-date information about devices (e.g., via a 510(k) summary database).

Recommendation: *CDRH should improve its mechanisms for leveraging external scientific expertise.*

Recommendation: *The Task Force recommends that CDRH, consistent with the Center's FY 2010 Strategic Priorities, develop a web-based network of external experts, using social media technology, in order to appropriately and efficiently leverage external expertise that can help Center staff better understand novel technologies, address scientific questions, and enhance the Center's scientific capabilities.*

AdvaMed encourages FDA to establish access to a wide range of experts, including medical and diagnostic experts who understand the medicine and technology of devices. On page 8 of the Report, the Task Force expresses a finding that, "it is difficult for Center staff to tap meaningful external scientific expertise in a timely manner." The Report then recommends that FDA establish a web-based system to enable staff to interact effectively with appropriate external experts. This recommendation partially parallels a similar recommendation that AdvaMed made during the discussions of FDA's use of science in decision making and the review of the 510(k) process. Despite our belief that both FDA and industry will be well-served if FDA staff can consult with external experts, we have several concerns that can be addressed at the beginning of the process design.

The term "social media technology" is unclear to us. Social media have become an enticing Internet venue serving a variety of purposes, some positive, others negative. Social media sites also have exhibited significant security problems. While we do not believe that FDA plans to consult scientists using current, publicly-available sites, we do believe that FDA must define the goals and the parameters, especially the limits, of the anticipated interactions.

Clearly, if external experts are to be consulted on scientific issues during a product review, the consultation is likely to include a discussion of trade secrets, proprietary information, or both. FDA should establish a defined process for choosing and qualifying external experts and for ensuring that the interactions are properly scoped, limited, and balanced. FDA should ensure that input from external experts are documented in reviewer decision summaries. FDA also should ensure confidentiality of communications related to reviews. Therefore, it is vital that the system design requirements include both a high level of cyber security, secure user access controls and other administrative, technical, and physical safeguards to protect the confidentiality of the data and to prevent unauthorized use or access. These safeguards should provide the same level and scope of security as safeguards for other federal government information systems.[20] It will be both easier and less expensive to include these controls at the beginning of development as opposed to adding them along the way.

There also is concern about potential conflicts of interest. Conflict of interest applies not only to industry ties but also to academic interests and reputation. It is important to balance the vetting process to ensure a large pool of experts while also minimizing bias. The selection process for choosing external experts for the web-based network, and the names of external experts and their qualifications should be made available on the FDA website to add transparency to the process. Additionally, developing a process to ensure transparency to the sponsor when CDRH is consulting external experts is a necessary step.

Recommendation: *CDRH should establish and adhere to as predictable an approach as practical for determining what action, if any, is warranted with respect to a particular product or group of products on the basis of new scientific information.*

Recommendation: *The Task Force recommends that CDRH assess best-practices for staff engagement with external experts and develop standard business processes for the appropriate use of external experts to assure consistency and address issues of potential bias. As part of this process, the Center should explore mechanisms, such as site visits, through which staff can meaningfully engage with and learn from experts in a variety of relevant areas, including*

[20] *See, for example*, Office of Management and Budget (OMB) Circular No. A-130, Appendix III--Security of Federal Automated Information Systems (http://www.whitehouse.gov/omb/circulars/a130/a130.html), Federal Information Processing Standard 200 "Minimum Security Requirements for Federal Information and Information Systems" (http://csrc.nist.gov/publications/fips/fips200/FIPS-200-final-march.pdf), and Special Publication 800-53 "Recommended Security Controls for Federal Information Systems" (http://csrc.nist.gov/publications/nistpubs/800-53-Rev2/sp800-53-rev2 final.pdf).

clinical care. In addition to supporting interaction at the employee level, the Center should also work to establish enduring collaborative relationships with other science-led organizations.

AdvaMed supports this recommendation. AdvaMed member companies encourage visits by FDA to healthcare facilities where they may observe the use of medical devices and *in vitro* diagnostics by actual users of the devices.

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

There is a lack of clarity within and outside of CDRH about when new scientific information warrants certain types of action by the Center, particularly a change in premarket evidentiary standards.

Recommendation: *The Task Force recommends that CDRH develop and implement a business process for responding to new scientific information in alignment with a conceptual framework comprised of four basic steps: (1) detection of new scientific information; (2) escalation of that information for broader discussion with others; (3) collaborative deliberation about how to respond; and (4) action commensurate to the circumstance — including, potentially, deciding to take no immediate action. As it puts this approach into practice, CDRH should consider adopting several key principles. First, the process should allow for a range of individuals to participate in the deliberation phase, including managers and employees, to help take into consideration potentially cross-cutting issues and assure consistency in responding to new scientific information. To support this principle, CDRH should establish a Center Science Council, comprised of experienced employees and managers and under the direction of the Deputy Center Director for Science, to provide oversight and help assure consistency across the Center. Second, the process should be streamlined to allow for new information to be raised and addressed in a timely manner. Third, the process should include a mechanism for capturing in a structured manner the rationale for taking a particular course of action, so that it can be articulated clearly to staff and external constituencies and incorporated into the Center's institutional knowledge base. Fourth, the process should be designed to allow for prioritization of issues. The Center should also develop metrics to determine whether or not the new process is effective.*

It is essential that CDRH prospectively establish a process for determining what action, if any, should be taken when new information on product performance is made available. AdvaMed supports the development of the "Predictable Approach" framework for responding to new scientific information. The four basic steps, outlined by FDA, are an appropriate means of rationally and consistently managing new information that comes to light after products have been placed on the market. However, a critical first step is to assess whether the new information is scientifically valid or simply information that may not be verified or verifiable. Such assessments will govern what, if any, actions should be taken. We also agree with a key principle articulated by FDA, that the framework should allow for "a range of individuals to

participate in the deliberation phase. It is imperative, however, that this range of individuals includes representatives from industry that are the most knowledgeable in the design, manufacture, and distribution of the product in question. Similarly, it would be appropriate for the users of the product in question to be consulted during the deliberation phase.
Finally we concur that the framework should include a mechanism for capturing in a structured manner the rationale for taking a particular course of action, so that it can be articulated clearly to FDA staff and external constituencies and incorporated into the CDRH institutional knowledge base.

Recommendation: *The Task Force recommends that CDRH enhance its data sources, methods, and capabilities to support evidence synthesis and quantitative decision making as a long-term goal.*

AdvaMed supports this recommendation. CDRH must have the tools, knowledge and resources available to support their mission and goals.

3. Promptly Communicating Current or Evolving Thinking to All Affected 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. For example, CDRH should explore 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. CDRH should also encourage industry and other constituencies to submit proposed guidance documents, which could help Center staff develop Agency guidance more quickly.*

AdvaMed supports the development of additional product specific guidance for FDA staff and industry. The increased issuance of Level 1-Immediately in Effect guidance, however, raises concerns about implementation of new expectations without adequate notice to affected stakeholders. In the real world of product submission development, 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 of 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-Immediately in Effect guidance seem to be modest and deny the full and rich exchange on information resulting from 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, 21 C.F.R. 10.115(d)(3), and are relied upon by FDA review staff, device companies and other stakeholders. 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. Currently, manufacturers typically learn of such changes through individual engagement with the Agency, often not until after they have prepared a premarket submission. The aim of issuing a "Notice to Industry" letter would be to provide greater clarity to manufacturers, in a timelier manner, about the Center's evolving expectations with respect to a particular group of devices. Because a change in regulatory expectations would represent a change in policy, a "Notice to Industry" letter would likely be considered guidance, although it would typically be issued relatively quickly and would generally not contain the level of detail traditionally found in other guidance documents. In the interest of rapidly communicating the Center's current regulatory expectations to industry, CDRH would generally issue "Notice to Industry" letters, if such letters constitute guidance, as "Level 1 – Immediately in Effect" guidance documents, and would open a public docket in conjunction with their issuance through a notice of availability in the Federal Register. To expedite the issuance of "Notice to Industry" letters, CDRH should develop standardized templates for these letters and, as necessary, their accompanying Federal Register notices. In addition, when appropriate, CDRH should follow "Notice to Industry" letters as soon as possible with new or modified guidance explaining the Center's new regulatory expectations in greater detail and revising the guidance where necessary in response to comments received, so that external constituencies have a fuller understanding of the Center's current thinking. CDRH should also consider creating a webpage for identifying and explaining*

new information that has altered the Center's regulatory expectations, so that, across all CDRH-regulated products, external constituencies can better understand the rationale for changes in the Center's requirements.

Although we support the Agency's recommendation to establish a standard practice for Notice to Industry (NTI) letters for use in conveying information for which the Center has changed its regulatory expectations on the basis of new information, we have several concerns and recommendations.

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 individually to companies with products already under review. Overuse of NTIs to communicate procedural topics, such as application format, or other topics that could be addressed via Level 2 guidance will reduce 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 recognition that whenever 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 expectations, accepting alternate but equivalent measures and establishing implementation dates. 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, as recommended by the Task Force, we recommend that 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 within a specified period of time.

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 tools to communicate to the industry in general, so that companies contemplating moving into the particular device market 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 information 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.

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 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(described further in Section 3, below).*

AdvaMed does not support the development of an on-line labeling repository. AdvaMed has expressed concerns about the feasibility and value of this recommendation in a previous comment. Further, without an understanding of FDA□s intent regarding the improvement of device labeling, we cannot support this proposal at this time.

Recommendation: *CDRH should provide additional information to its external constituencies about its process for determining an appropriate response to new science and the bases for its actions.*

Recommendation: *The Task Force recommends that CDRH 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. The SOP should include the expectation that when a decision is made to take a particular course of action, including a change in evidentiary expectations, the action and its basis should be communicated clearly and promptly to all affected parties. If it is not possible to provide complete detail about the basis for an action due to confidentiality concerns, Center staff should share as full an explanation as is allowable and state why a more complete explanation is not permissible. In addition, Center leadership should take steps to make sure that all employees have an accurate understanding of what information they are permitted to discuss with manufacturers, so that information that would help clarify the basis for a particular action is not needlessly withheld.*

AdvaMed suggests that all stakeholders be involved in developing the standard operating procedure. As with any process that involves and impacts multiple groups, acceptance of and conformance to the process improves when all stakeholders are involved. Importantly, the

principles we outlined in our response to the conceptual framework proposal, should also be applied to any SOPs.

Recommendation: *The Task Force recommends that CDRH continue its ongoing efforts to make more meaningful and up-to-date information about its regulated products available and accessible to the public through the CDRH Transparency Website, consistent with the Center's FY 2010 Strategic Priorities and the work of the FDA Transparency Task Force. In addition to the pre- and postmarket information that is already available on CDRH Transparency Website, the Center should move to release summaries of premarket review decisions it does not currently make public (e.g., ODE 510(k) review summaries) and make public the results of post-approval and Section 522 studies that the Center may legally disclose. Making such information readily available to the public will provide CDRH's external constituencies with greater insight into the data that guide the Center's decisions and evolving thinking.*

As stated in our previous comments, AdvaMed supports the posting of reviewer summaries on a CDRH website, however, only those summaries for cleared devices should be released. Review summaries for devices that are not cleared would reveal company confidential information that would negatively impact marketing competitiveness and at the same time, serve no public health benefit because the product has not yet been made available to the public. An NSE determination is not the end of a company's product development. A company may resubmit the 510(k), pursue the *de novo* pathway, or submit a PMA. AdvaMed has submitted detailed comments on FDA's transparency initiative (see AdvaMed comments at Docket No. FDA-20098-N-0247) that articulate our strong concerns about FDA's proposed disclosure of confidential and proprietary information. For these reasons, AdvaMed supports making public only summaries of the results of post-approval and Section 522 studies that the Center may *legally* disclose.

ATTACHMENT A

Battelle
The Business of Innovation

510(k) Premarket Notification Evaluation

Prepared By:
Battelle Memorial Institute

For:
AdvaMed

September 2010

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510(k) Premarket Notification Evaluation

1. Introduction

This report analyzes Class I recalls of medical devices which were previously cleared through the United States Food and Drug Administration's (FDA's) 510(k) Premarket Notification Process. These recalls are compared to recalls of exempted devices as well as devices approved through the Premarket Approval (PMA) process. Data were gathered from publically available information from the FDA, as well as information made available by companies with affected products.

2. Executive Summary

FDA product recalls are actions taken when FDA-regulated products are defective or potentially harmful; Class I recalls are the most serious of these recalls, and represent products that may cause serious health problems or death. Data for Class I recalls of 510(k)-cleared devices in the United States were reviewed over a 64-month period, beginning January 1, 2005 and ending May 1, 2010 (hereafter referred to as the ~~"r~~review period"). There were, on average, 15 unique 510(k)-cleared device recalls per year between calendar years 2005 and 2009.

There have been 46,690 devices cleared through the 510(k) process since 1998—the year certain low-risk medical devices began to be exempted from premarket notification requirements (as part of The Food and Drug Administration Modernization Act (FDAMA)). This time period was selected because gathering data back to 1976 (the enactment of the 510(k) process) would include a large number of Class I devices which were later exempted from the 510(k) process by the FDAMA. This would inflate the total number of devices cleared, reducing the percentage of significant recalls for devices. The number of clearances/approvals from 1998 through May, 2010 was used to calculate recall percentages because it was assumed to be more representative of the number of products on the market potentially subject to recall rather than only using products cleared during the 64-month review period.

In this same time period since 1998, 2,825 devices have been approved through the Premarket Approval (PMA) process. This total includes PMA supplements representing significant changes: 180-day supplements and panel track supplements. 180-day supplements which are categorized as ~~"n~~o user fee" are excluded, as these filings are generally for minor changes such as manufacturing location or labeling which improves or clarifies warnings or precautions.

The table below details the number of devices with recalls over the review period of January 1, 2005, to May 1, 2010. Because the enactment date of FDAMA was used to calculate the total number of devices cleared or approved, recalled devices that were cleared or approved prior to the enactment of FDAMA were excluded from the total recall count and percentage calculations. Recalls of both 510(k)-cleared and PMA-approved devices represent a fraction of a percent of all total clearances or approvals, and a smaller percentage of recalls have been associated with 510(k) clearances than with PMAs (0.16% vs. 0.85%).

Number of Cleared or Approved Devices Recalled, Compared to all Clearances and Approvals Since 1998

Clearance or Approval Type	Total Number of Devices Cleared or Approved Since 1998	Class I Recalls: Jan. 2005 – May 2010	Percentage of Total
Devices - PMA	2,825[1]	24	**0.85%**
Devices - 510(k)	46,690	77	**0.16%**

Probable causes of device recalls were assessed based on available data from manufacturers and the FDA. Several assumptions were made in this assessment, and are detailed in Sections 3 and 5. According to this analysis, approximately 50% of the recall causes of 510(k)-cleared devices in the review period were attributed to design deficiencies (representing less than 0.1% of all 510(k) clearances since 1998), 29% to manufacturing deficiencies, and 6% to labeling deficiencies. The remaining 15% of 510(k)-cleared device recall causes were classified as ~~d~~design or manufacturing," as data were not available to make a determination with a reasonable degree of confidence.

In the United States, medical devices are classified into three classes, Class I, II, and III, based on the level of control necessary to assure the safety and effectiveness of the device. Recalls of Class II devices represent 61% of all device recalls over the review period, followed by Class III devices at 28%. Class III devices, which primarily follow a PMA approval pathway, have recently (CY 2004-2008) represented approximately 15% of device approval and clearance totals at the FDA. This percentage includes both original PMA applications (1%) and supplements to PMA approvals (14%), with 510(k)s for Class I, II, and III devices constituting the remaining 85%.

In summary, devices cleared through the 510(k) Premarket Notification Process result in a smaller percentage of recalls (0.16%) than PMA approved devices (0.85%), and these recalls represent a fraction of a percent of all devices cleared or approved since enactment of the FDAMA.

More detailed results of the analysis, including charts and tables, are contained in Section 3. Assumptions made in the data analysis and data collection methods are detailed in Section 5.

[1] Includes 180-day supplements (excluding "no user fee" supplements) and panel track supplements.

3. Recalls of Devices Cleared through the 510(k) Premarket Notification Evaluation

Recalls are actions by a device manufacturer to correct a problem or remove a product from the market. Class I recalls are the most serious recalls, and involve a *"situation in which there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death*[2]*".* Recalls may be conducted on a manufacturer's own initiative, by FDA request, or by FDA order under statutory authority. Class I recalls can be issued for medical devices, drugs, biologics, and food. Only a portion of medical device recalls are for devices that have been cleared through the 510(k) Premarket Notification Process.

Recall data for 510(k)-cleared devices were evaluated over an approximate five year review period, from January 1, 2005 to May 1, 2010. Recalls of PMA-approved devices are referenced for comparative purposes.

3.1. Number of Unique Recalls

United States Class I medical device recalls were gathered from the FDA's "Medical Device Recalls" database[3] on May 6, 2010, resulting in several hundred line-item recalls. Some line item recalls were then grouped with similar entries. This grouping methodology is outlined below:

- Recalls were grouped when different model numbers of the same product were recalled, provided the products were likely marketed under the same 510(k) or PMA and involved the same root cause.
- Recalls were grouped when products were re-branded for sale under different trade names, provided the products were likely marketed under the same 510(k) or PMA and involved the same root cause.
- Recalls were grouped when a recall was expanded to additional manufacturing lots of the same product for the same root cause.
- Recalls were grouped when a recall involved a single manufacturer for systemic production or quality issues over a limited time period. For example, a failure to follow Good Manufacturing Practices[4] (GMP) across several product lines.

The FDA's weekly "Enforcement Reports"[5] and the FDA's "list of Device Recalls"[6] were used to aid in this grouping process.

Device recalls were then categorized based on the devices' likely clearance or approval histories, using data available in the FDA's PMA and 510(k) databases.

Figure 1 compares the total number of Class I recalls for 510(k)-cleared devices with other device recalls over the review period of January 1, 2005, to May 1, 2010. "Other Devices" includes devices exempt from Premarket Notification or Approval, or devices marketed without receiving an appropriate clearance, approval, or exemption.

[2] United States Code of Federal Regulations, 21 CFR 7.41.
[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm
[4] United States Code of Federal Regulations, 21 CFR 110.
[5] http://www.fda.gov/Safety/Recalls/EnforcementReports/default.htm
[6] http://www.fda.gov/medicaldevices/safety/recallscorrectionsremovals/listofrecalls/default.htm

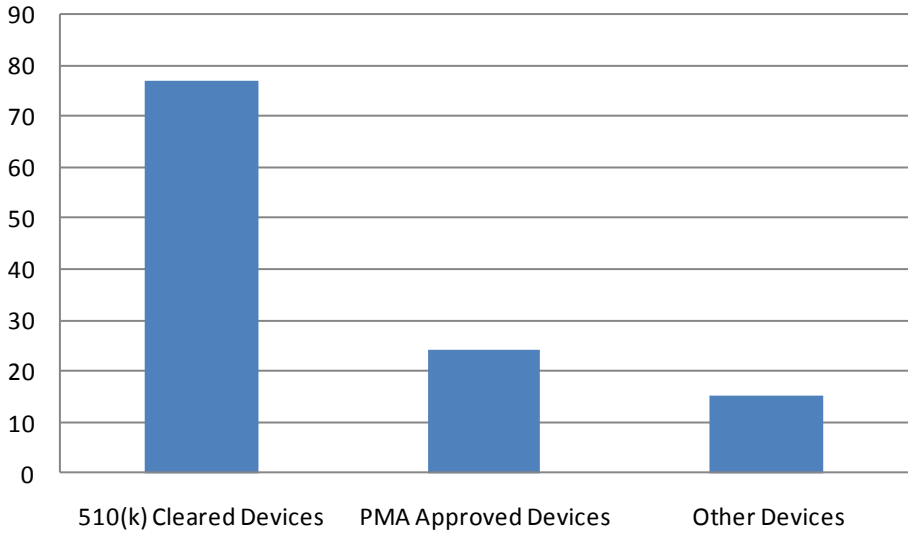

Figure 1: Number of Device Recalls.

3.2. Number of Class I Recalls Compared to the Total Number of Products Cleared or Approved

The total numbers of device clearances and approvals since 1998 were used as relative indications of the respective number of devices on the market. In 1997, the U.S. enacted the Food and Drug Administration Modernization Act (FDAMA), which represents the last major change to the FDA's clearance and approval regulations, and included a 510(k) filing exemption for certain low risk medical devices (e.g. tongue depressors). This premarket notification exemption was implemented in early 1998[7]. Table 1 below displays the percentage of devices recalled during the review period as compared to the total number cleared or approved since 1998. Devices with 510(k) clearances represent the smallest percentage of Class I recalls when compared to the total number of clearances or approvals. The PMA totals include both PMAs and PMA supplements representing significant changes: 180-day PMA supplements (excluding ~~-no~~ user fee" supplements) and panel track supplements.

Table 1: Number of Cleared or Approved Devices Recalled, Compared to all Clearances and Approvals Since 1998.

Clearance or Approval Type	Total Number of Devices Cleared or Approved Since 1998	Class I Recalls: Jan. 2005 – May 2010	Percentage of Total
Devices – PMA	2,825[8]	24	**0.85%**
Devices - 510(k)	46,690	77	**0.16%**

[7] On February 2, 1998, the FDA published a notice in the Federal Register announcing a list of Class I devices that it considered to be exempt from premarket notification effective February 19, 1998.
[8] Includes 180-day supplements (excluding "no user fee" supplements) and panel track supplements.

3.3. Device Recall Causes

This section presents the most likely causes of Class I recalls for 510(k)-cleared and PMA-approved devices, based on available data.

The determination of cause for some recalls was straightforward, such as a ~~"m~~manufacturing" cause for a device manufactured without following Good Manufacturing Practices (GMP). Other cause determinations had to be inferred through often limited information available in the recall text, press releases, and the manufacturers' published data. The ~~"A~~Assumptions" section, Section 5.1, details these uncertainties in greater detail.

The cause categories used for the device analysis are detailed below:

Manufacturing
These recalls include causes that were most likely related to manufacturing deficiencies. These causes may include failure to maintain sterility, failure to follow GMP, or manufacturing QC deficiencies.

Design
These recalls include causes that are likely due to flaws inherent in the design of the device, either created initially or through approved design changes (e.g., part obsolescence).

Manufacturing or Design
Recalls in this category could either be due to manufacturing or design causes. The information available for these recalls does not indicate the cause of the recall, other than the root cause was likely either in design or manufacturing. This category was employed due to frequent lack of comprehensive information provided by the FDA's recall notice and the device manufacturers. An example may include a failed electronic component, where no data are given as to why it failed; the component failure may be tied to the initial design not accounting for tolerances, or a supplier quality issue delivering out-of-specification components.

Labeling
These recalls result from a labeling deficiency (though these issues may ultimately result from a manufacturing or a design root cause).

Table 2 presents the likely cause of Class I recalls for 510(k)-cleared and PMA-approved devices, using the categories mentioned above. These causes are presented as a percentage of total devices marketed since 1998. As previously mentioned, total PMA devices include panel track supplements and 180-day supplements, excluding ~~"n~~o user fee" supplements. The analyses include recalls issued between January 1, 2005, and May 1, 2010.

Table 2: Percentage of Device Recall Causes, Compared to Total Number of Devices Cleared or Approved Since 1998.

Clearance or Approval Type	Recalls as a Percentage of Total Devices Since 1998	Recalls due to Design Causes	Recalls due to Manufacturing Causes	Recalls due to Labeling Causes	Recalls due to Manufacturing or Design Causes
Devices - PMA	**0.85%**	**0.46%**	**0.18%**	**0.11%**	**0.11%**
Devices - 510(k)	**0.16%**	**0.08%**	**0.05%**	**0.01%**	**0.03%**

3.4. Device Recall Requirements

A variety of impacts to devices currently on the market can occur when a Class I recall is initiated. Four categories were used in this research:

Removal from Inventory:
The device under recall was required to be removed from operation. The methods included destroying devices, returning devices to the manufacturer, or on-site removal by the manufacturer. Often, refurbished or replacement devices were provided to the customers.

Field Fix:
The device under recall could be repaired in the field, either by the manufacturer or the user. These fixes often included software upgrades or replacement components.

Labeling:
These recalls addressed a product deficiency which could be mitigated with a labeling change. Recalls initiating a labeling change may provide labeling updates electronically, through mail, or through an on-site call by the manufacturer.

Monitor for Conditions:
The requirements for these recalls included the monitoring of patients or equipment for adverse events. This included monitoring patients with potentially defective implantable devices.

Figure 2 outlines the field requirements of Class I 510(k) device recalls and Figure 3 outlines the field requirements of Class I PMA device recalls, using the categories outlined above. The review period was January 1, 2005, to May 1, 2010.

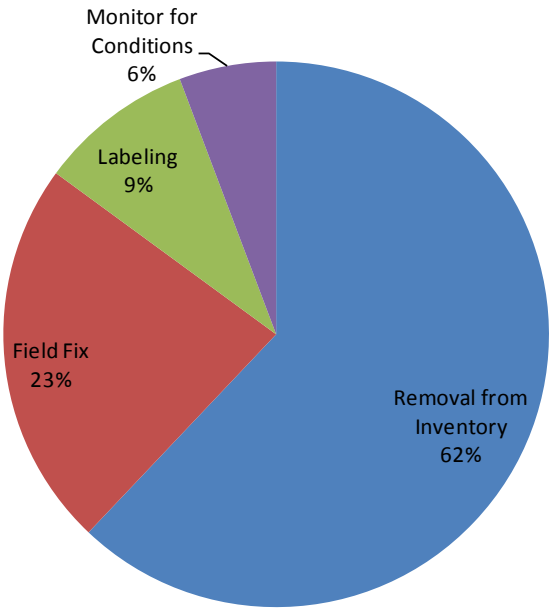

Figure 2: Field Requirements for Class I 510(k) Device Recalls.

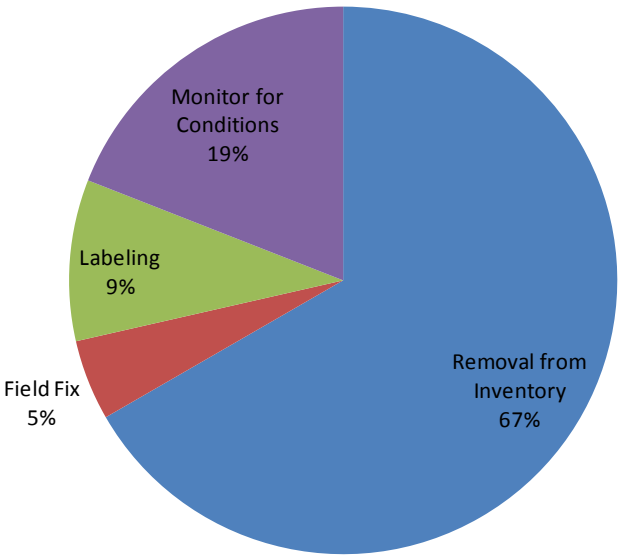

Figure 3: Field Requirements for Class I PMA Device Recalls.

3.5. Clearance and Approval History of Recalled Devices

Clearance or Approval Type

Devices that have undergone a Class I recall meet one of the following four conditions:

- The device has been cleared through the 510(k) process (Special, Traditional, or Abbreviated 510(k)).
- The device has been approved through a Premarket Approval Application (PMA).
- The device has been exempted from clearance or approval because the device is one that was in commercial distribution before May 28, 1976, the enactment date of the Medical Device Amendments.
- The device was not cleared, approved, or exempted through any of the three pathways above.

The 510(k) or PMAs associated with the recall could not always be identified with a high degree of confidence, as manufacturers and model numbers may change without notification to the FDA. In addition, manufacturers may have renamed the product or produced derivative products that did not require a separate filing. The ~~"A~~ssumptions" section, Section 5.1, details the methodology and assumptions used to determine the most likely 510(k) or PMA associated with the recall. Figure 4 indicates the clearance / approval history of the Class I recalled devices over the review period.

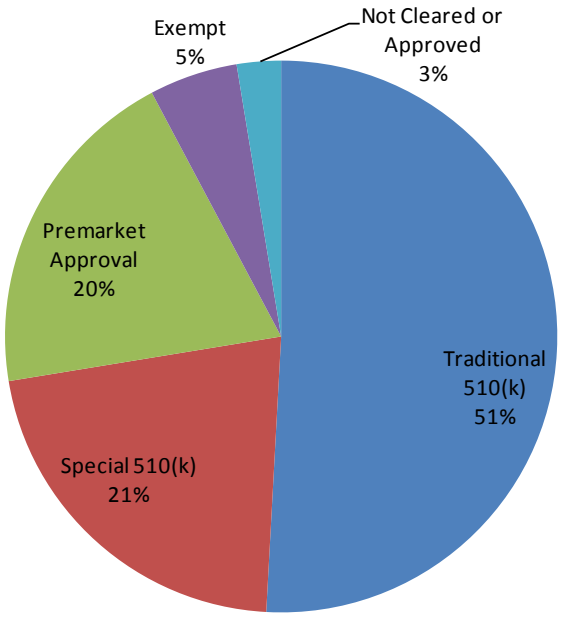

Figure 4: Clearance/Approval Routes of Class I Device Recalls.

3.6. Device Class and Type Recalled

This section documents Class I recalls by device classification, according to the FDA's classification system. The FDA has established classifications for roughly 1,700 medical devices and grouped them into 16 device panels. Each of these generic types of devices is assigned to one of three regulatory classes (I, II, or III), based on the level of control necessary to assure the safety and effectiveness of the device. Data are based off the 510(k) or PMA associated with the recalls.

Device Classification

The three U.S. medical device classes and the requirements which apply to them are:

- Class I: (General Controls)
  - With Exemptions
  - Without Exemptions
- Class II: (General Controls and Special Controls)
  - With Exemptions
  - Without Exemptions
- Class III: (General Controls and Premarket Approval)

The class to which a device is assigned determines, among other things, the type of premarketing submission/application required for FDA clearance to market. If the device is classified as Class I or II, and if it is not exempt, a 510(k) is required for marketing. All devices classified as exempt are subject to the limitations on exemptions[9]. For Class III devices, a premarket approval application (PMA) is required unless the device is on the market prior to the passage of the medical device amendments in 1976, or substantially equivalent to such a device (and PMA's have not been called for).

Figure 5 displays the device classification of Class I recalled devices over the review period. Figure 6 shows the percentage of devices cleared or approved over a 5 year period from 2004 through 2008[10] for comparative purposes; however, no data are available to indicate the number of preamendment or 510(k) exempt products placed on the market in this timeframe.

[9] Limitations of device exemptions are covered under 21 CFR xxx.9, where xxx refers to Parts 862-892.
[10] FDA ODE, Annual Performance Report, FY 2008.

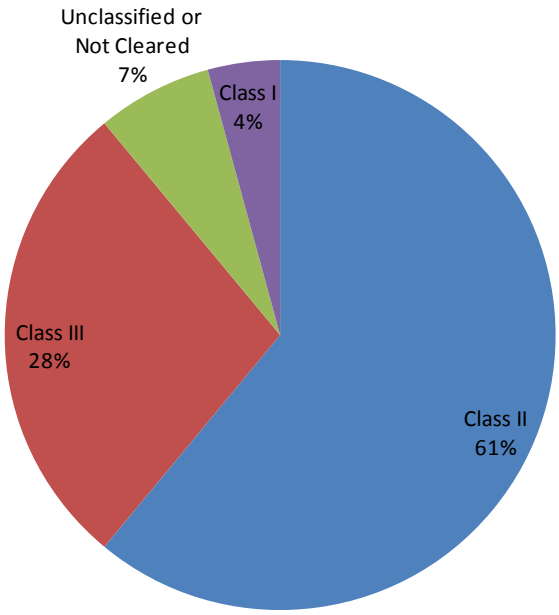

Figure 5: Device Classification of Class I Recalls.

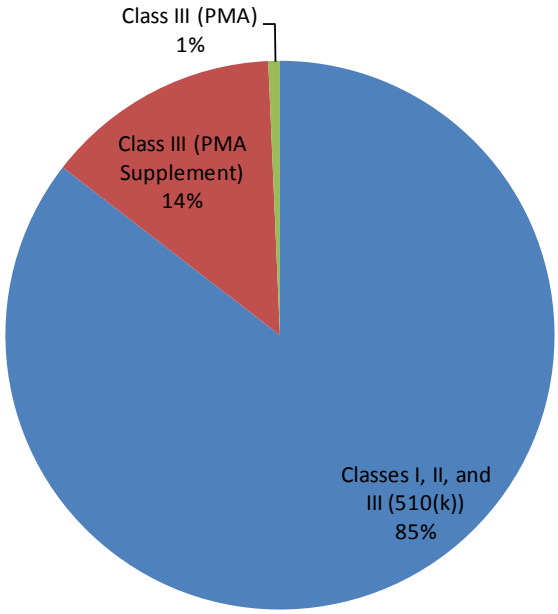

Figure 6: Device Classification of All Clearances and Approvals, FY 2004-2008 (FDA).

4. Conclusion

The number of devices with post-FDAMA 510(k) clearances that have undergone a Class I recall between January 1, 2005 and May 1, 2010—approximately 77—represents less than 0.16% of the 46,690 devices that have been cleared through the 510(k) Premarket Notification Process since 1998. This represents a significantly smaller percentage than Class I recalls of PMA approved devices at 0.85%.

5. Appendices

5.1. Assumptions

The following list outlines key assumptions made while collecting and analyzing the data presented in this report.

1. Data were based on publicly available information on the FDA's website, www.fda.gov, and a limited number of press releases and news external to the FDA's website. Data were collected from May 6, 2010 to May 26, 2010. Data from these sources were assumed to be accurate and complete.

2. Recall data—including letters to medical professionals, press releases, enforcement reports, and supplementary information—did not include data on the devices' clearance or approval histories. Therefore, the authors had to surmise the most likely 510(k) or PMA associated with each recall. In many cases, trade names and manufacturers listed in the device recalls are not the same as those listed in the devices' 510(k)s and PMAs, due in part to mergers, acquisitions, or re-branding.

3. In a majority of cases, recall data—including letters to medical professionals, press releases, enforcement reports, and supplementary information—did not provide adequate data to determine with certainty the root cause of the device recalls. In particular, determining cause between "design" and "manufacturing" was particularly uncertain; in many cases the authors had to surmise the most likely cause of the recall, or bin the data into a combined group—"Design or Manufacturing". Certain rules were used to assign recalls to particular categories. These include:

    - Failure to maintain or assure sterility: manufacturing.
    - Failure to follow GMP: manufacturing.
    - All labeling issues: labeling (whether root cause was design or manufacturing).
    - Software "bug" (except where due to failure in software manufacturing processes): design.
    - Recall of specific lots of an established product: manufacturing.

4. Similar line item recalls across a limited date range were considered to be a single recall. For example, cases where a recall was expanded to additional lots or product lines were considered to be a single recall.

5. Approximately 5% of device recalls which were not associated with preamendment or exempt devices could not be associated with a 510(k) or PMA with a reasonable degree of certainty. These recalls were not included in the tally of device class, but were included in the count of number of medical device recalls per year.

6. Because the enactment date of FDAMA was used to calculate the total number of devices cleared or approved, recalled devices that were cleared or approved prior to the enactment of FDAMA were excluded from the total recall count and percentage calculations.

5.2. Data Sources and Collection Methods

On May 6, 2010, an initial list of Class I device recalls was queried from the database located at:

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm

The following search parameters were selected:

- Product name: blank
- Recall class: 1
- Recall number: blank
- Reason for recall: blank
- Recalling firm: blank
- Sort by: Date Record Posted (Descending).

From this list, recalls were combined into logical groupings, based on recall text and other available data, including the "Recall Summary" page, located at:

http://www.fda.gov/medicaldevices/safety/recallscorrectionsremovals/listofrecalls/default.htm

Once recalls were recorded and grouped, 510(k)s and PMAs associated with the recalls were researched.

For 510(k)s, the primary method of research included searching the FDA website for 510(k) summary information through an external search engine (Google). The following example search demonstrates the format that was used:

```
site:fda.gov filetype:pdf 510(k) Guidant pacemaker
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For PMAs, the FDA's PMA database was used for research, as well as search engine queries:

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

After an initial list of potential 510(k)s and PMAs were determined, the search was narrowed and modified to key-in on specific model names or features that were present in the recalled

devices. Company websites, literature, and published information were used to gain confidence that the appropriate 510(k) or PMA was selected.

Once the 510(k) or PMA had been selected, information was recorded from the submission and clearance/approval, including device classification and panel, clearance/approval date, and clearance/approval route.

ATTACHMENT B

AdvaMed
Advanced Medical Technology Association

AdvaMed Legal Analysis of Rescission Authority

In its proposal, 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.

510(k) Working Group Preliminary Report and Recommendations at 58. Under current law, FDA does not have statutory authority to rescind a 510(k) substantial equivalence determination, and this authority cannot be implied from policy or other non-statutory grounds. Consequently, without a basis in the Federal Food, Drug, and Cosmetic Act (FD□C Act), the agency cannot promulgate regulations defining rescission authority. FDA can only nullify a finding of substantial equivalence if the 510(k) applicant committed fraud in seeking that determination or, in very limited circumstances, based on inadvertent administrative mistakes or errors by the agency.

Rescinding a 510(k) would not only reclassify a device, but would reclassify all devices that relied upon the device subject to rescission, and would do so without adhering to the reclassification requirements in the FD□C Act for new devices, *see* □513(e). Effectively, the Working Group and the Center for Devices and Radiological Health (CDRH) are using so-called rescission as an enforcement tool for removing undesirable devices from the market, instead of removing such devices through the exercise of the agency□s substantial and broad enforcement authority. If the agency believes it is important to remove a device from use and eliminate it as a predicate, under the law what FDA must do is obtain a judicial order finding a device is misbranded or adulterated, thus, eliminating the device as a predicate in the premarket notification process, *see* □ 513(i)(2). Alternatively, FDA could reclassify the device into class III, assuming the administrative record would support reclassification. Rescission is unnecessary to protect the public health, and as we discuss below, neither the agency□s bases for rescission proposed in 2001, nor its current statements support or create rescission authority.

I. FDA DOES NOT HAVE STATUTORY AUTHORITY TO RESCIND 510(K)s BASED ON SUBSTANTIVE OR POLICY GROUNDS AND CANNOT PROMULGATE REGULATIONS DEFINING THAT AUTHORITY.

A. FDA does not have authority under the FD□C Act to rescind 510(k)s.

The FD□C Act does not directly or indirectly authorize FDA to rescind substantial equivalence orders. Under that Act, Congress explicitly gave FDA the authority to

withdraw premarket approvals (PMAs) (□515(e)(1)), investigational device exemptions (IDEs) (□520(g)(5)), and product development protocols (PDPs) (□515(f)(7)). The authority to classify devices under sections 510(k) and 513(f)(1) (and later 513(i)) did not include the authority to rescind classifications. Consistent with the rule of statutory construction, if the legislature did not include withdrawal or rescission authority, it was not intended. The FD□C Act□s remedy for an incorrect classification was and is reclassification. Indeed, Congress identified separate reclassification provisions for each group of devices that were subject to classification under the Act: preamendment devices and those substantially equivalent to them (□513(e)); postamendment class III devices (□513(f)(3)); and transitional devices (□520(l)(2)). No analog to withdrawal authority exists for premarket notification orders because these orders are not approvals, *see* 21 CFR □807.97 (deeming 510(k) devices misbranded when represented as receiving FDA approval), like the administrative orders that are subject to withdrawal.

Even the fact of an approval did not by itself imply the authority to withdraw an approval. In the drug context, Congress recognized that the power to approve does not imply the power to withdraw. Specifically, in 1938, it gave FDA the power to approve new drug applications (NDAs); in 1962, it gave FDA the power to withdraw such applications. The 1962 provision would have been unnecessary if the power to approve NDAs had included or implied the power to withdraw them. If an approval did not entail the power to withdraw the approval, certainly FDA cannot through a miracle of words create withdrawal or rescission authority for a classification, particularly when the statute explicitly provides for reclassification authority.

Because premarket notification under the FD□C Act is a means of classifying devices, rescinding a 510(k) clearance would reclassify that device. Reclassification of preamendment devices, including substantially equivalent devices, is governed by section 513(e) of the FD□C Act. That provision permits reclassification through rulemaking if FDA has □new information□to justify the result. Under section 513(e), FDA may reclassify a type of class III device into class II or class I, or may reclassify a type of class II device into class I. *See* 21 C.F.R. □860.130(c). Rescinding a 510(k) would reclassify substantially equivalent class I and II devices into class III. Consequently, if FDA asserts the authority to rescind a device□s marketing clearance for any reason, at any time, the agency would be substituting its judgment for that of Congress, and would change a device□s classification in a way not anticipated or permitted under the FD□C Act. Rescission of a 510(k) device classification would be an agency-created reclassification remedy without basis in the FD□C Act.

FDA cannot promulgate regulations that exceed the authority granted to it under the FD□C Act. Section 701(a) of that Act grants FDA □the authority to promulgate regulations for the efficient enforcement of [the FD□C Act].□ However, section 701(a) does not give FDA unlimited regulatory powers; □regulations issued under that section must effectuate a Congressional objective expressed elsewhere in the Act.□ *Pharm. Mfrs. Ass'n v. FDA*, 484 F.Supp. 1179, 1183 (D.Del. 1980), *aff'd* 634 F.2d 106 (3d Cir. 1980).

In *U.S. v. Nova Scotia Food Products*, 568 F.2d 240 (2d Cir. 1977), the U.S. Court of Appeals for the Second Circuit stated that section 701(a) of the FD□C Act is □analogous to the provision □make . . . such rules and regulations as may be necessary to carry out the provisions of this Act,□ in which case the □validity of a regulation promulgated thereunder will be sustained so long as it is □reasonably related to the purposes of the enabling legislation.□□ *Nova Scotia Food Prods.*, 568 F.2d at 246 (citations omitted). The U.S. District Court for the District of Columbia pointed out that section 701 of the FD□C Act □does not constitute an independent grant of authority that permits FDA to issue any regulation the agency determines would advance the public health. Rather, □[701] permits the FDA to use rules as a means of administering authorities otherwise delegated to it by the Congress.□ *Ass'n of Am. Physicians and Surgeons v. FDA*, 226 F.Supp.2d 204, 213 (D.D.C. 2002). Because the FD□C Act does not grant FDA the authority to rescind 510(k)s, none of the agency□s regulations can express or imply such authority.

In 2001, FDA asserted in a proposed rule that its administrative procedure regulations (specifically, 21 C.F.R. □□10.33(a), (h), and 10.75) provide the authority to rescind 510(k)s. *See* 66 Fed. Reg. 3523, 3524 (Jan. 16, 2001). It is improper for the agency to rely on a regulation as authority to issue another regulation. Indeed, FDA□s regulations cannot provide it with authority that was not conferred by Congress in the first place. Without authority from the FD□C Act, FDA cannot issue additional regulations to rescind 510(k) device classifications.

B. FDA does not have implied power to rescind 510(k)s.

Understanding there was no statutory basis for rescission, FDA in the past asserted its recession authority derived from federal case law that recognizes an implied authority for agencies to reconsider administrative actions, even if the applicable statutes and regulations do not provide for reconsideration. *See* 66 Fed. Reg. at 3524. However, that case law provides a narrow implied authority for tribunals to reconsider actions before the time for an appeal of the action has lapsed; it does not imply the authority to revoke a vested interest, such as a 510(k) classification determination. The cases make clear that the implied authority to reconsider a matter only exists until jurisdiction lapses, *i.e.*, a decision becomes final.

For example, in *West v. Standard Oil Company*, 278 U.S. 200 (1929), the U.S. Supreme Court ruled that the Secretary of Agriculture had authority to consider a dispute about the character of contested lands, notwithstanding that the Secretary had previously ordered a dispute over the lands dismissed. The Court□s holding that the order of dismissal was not a final act hinged on two factors. First, the Court found that the dismissal did not reflect a determination on the merits following a full evaluation of the facts. *See id.* at 213. Second, and more importantly, the Court determined that the dismissal did not result in a patent, or an instrument embodying a binding determination of rights in the land. *See id.* at 219 (after issuance of an order conferring rights, administrative findings of fact relied upon in issuing the order □are conclusive, in the absence of fraud or mistake□). For these

reasons, the Court found that no final order had issued, and jurisdiction remained with the Secretary. After jurisdiction lapses, however, there is no implied agency authority to reconsider and alter a previous order. *See Prieto v. United States*, 655 F. Supp. 1187 (D.D.C. 1987) (rejecting the Department of the Interior's revocation of the trust status of certain lands because the Department had failed to issue its reconsideration within the thirty day period permitted for appeals, and its jurisdiction over the trust status of the lands therefore ceased).

Timing is critical to an agency's ability to reconsider its actions. In *Albertson v. FCC*, a case frequently cited for the principle that "the power to reconsider is inherent in the power to decide," the reconsideration fell within the 20-day period permitted for an appeal of the administrative board's initial decision. *See* 182 F.2d 397, 399 (D.C. Cir. 1950). The *Albertson* court wrote: "the power of the Commission to hear and determine matters arising under the rehearing provision . . . carries with it by implication the authority to reconsider . . . within the twenty days allowed for an appeal. . . . That is so, for within such period jurisdiction over the contested order remains with the commission." *Id.* Thus, while this decision has occasionally been cited for a broad power of an agency to reconsider its actions, *see Civil Aeronautics Bd. v. Delta Airlines, Inc.*, 367 U.S. 316, 339 (1961) (dissenting opinion), the case in fact is a restatement of the principle of *Standard Oil* that an agency may reconsider its actions, but only before passage of time or other events render the action final.

Once FDA issues its substantial equivalence order, a device's classification and marketing status are final. On the day a substantial equivalence decision is received, the product could be marketed and the review process would lapse. At this stage, the case law FDA relies upon would bar a change in the device's classification status, except through a Congressionally-mandated statutory process. At best, FDA could argue that under "517(a)(8) of the FD"C Act it has 30 days until jurisdiction would lapse to reconsider a classification decision under section 510(k)/513(f)(1) because any interested party could appeal a substantial equivalence determination. Even if one accepted this view, FDA's authority to reconsider a premarket notification classification decision would lapse after 30 days, coincidental with the expiration of the time period for an appeal.

In sum, FDA simply cannot rely on the principle of an implied power of reconsideration to authorize rescission at any time after the agency issues an order of substantial equivalence. Such a rule would be unlawful because it would effectively deny finality to any FDA order, and would be at odds with judicial authority that unequivocally states that an agency's jurisdiction to reconsider a matter ceases when an order becomes final. Although FDA could argue that a substantial equivalence order remains open until all appeal rights are extinguished, even then the agency would have only 30 days to reconsider a premarket notification classification order.

II. FDA CAN ONLY NULLIFY A FINDING OF SUBSTANTIAL EQUIVALENCE IN CASES OF FRAUD OR ADMINISTRATIVE MISTAKE OR ERROR.

As the 510(k) Working Group points out in its CDRH Preliminary Internal Evaluations Report, "agencies have inherent authority to reconsider their decisions in certain circumstances, such as where there has been fraud or error, and to rectify their mistakes." 510(k) Working Group Preliminary Report and Recommendation at 58. However, this authority does not create a basis for 510(k) rescission authority. Rather, it allows the agency to nullify substantial equivalence determinations in the rare case of fraud or administrative mistake or error.

For example, in *American Trucking Association v. Frisco Transportation Company*, 358 U.S. 133 (1958), the U.S. Supreme Court rested its ruling that an administrative agency may correct inadvertent errors in its decision-making upon a factual finding that the Interstate Commerce Commission's failure to specifically reserve authority in trucking certificates to cancel the certificates was clerical inadvertence or mistake rather than a policy change. 358 U.S. at 146. This principle would permit FDA to reconsider, without express statutory authority, any decision reflecting clerical errors, for example, were a reviewer to inadvertently omit the letter "N" before "SE." The principle does not, however, permit the agency to rescind a substantial equivalence determination on substantive grounds, for example, an agency reassessment of data or receipt of new safety and effectiveness information that put in question a prior determination. *See Concerned Citizens of Bridesburg v. EPA*, 836 F.2d 777, 786 (3d Cir. 1987) (distinguishing typographical errors from substantive agency determinations resulting in approvals).

The 510(k) Working Group cites *American Therapeutics Institute v. Sullivan*, 755 F. Supp. 1 (D.D.C. 1990), as authority that agencies can reconsider decisions in certain circumstances. The decision in *American Therapeutics Institute* is consistent with the line of cases construing a narrow administrative authority to reopen orders that may be legitimately characterized as mistakes. Specifically, the court dismissed a pharmaceutical company's case against FDA challenging the agency's summary rescission of an NDA six weeks after its issuance on grounds of inadvertence because FDA rescinded on the basis of information that existed at the time of the approval and that, if known by the reviewing official during the application's review, would have resulted in disapproval. However, the court's holding only reflects the determination that the agency's use of rescission shortly following an inadvertent error was not so clearly ultra vires as to justify its intervention in a matter properly resolved by the court of appeals, which had exclusive jurisdiction to hear appeals of NDA denials under section 505(h) of the FD"C Act. *See id.* at 2. Far from establishing a precedent permitting 510(k) rescission, the case is extremely limited and only demonstrates the reluctance of a district court to intervene in a statutorily-defined appeals scheme after determining that the case presented "an unresolved issue of statutory interpretation and administrative law within the exclusive jurisdiction of the Court of Appeals." *Id.* The district court determined it was without

jurisdiction to grant relief against the government, unless FDA's action was clearly beyond the scope of its authority, and that the court of appeals had exclusive jurisdiction to determine whether the agency's denial of an NDA was lawful.

Importantly, courts have taken strong exception to attempts by agencies to change past actions through purported corrections of mistakes based upon inadvertence or fraud as a means to legitimize changes in policy. For example, in *Prieto v. United States*, 655 F. Supp. 1187 (D.D.C. 1987), the court wrote that "perhaps the most compelling reason" of several for rejecting the attempted revocation of a trust status was the Department of Interior's pretext in relying on an unfounded assertion of fraud to "bootstrap de novo review" of its initial determination. *Prieto*, 655 F. Supp. at 1192. In another illustrative case, after reviewing a record that clearly demonstrated a policy change, the court in *Concerned Citizens of Bridesburg v. EPA*, 836 F.2d 777 (3d Cir. 1987), rejected EPA's efforts to characterize approvals of state odor provisions as "inadvertent" where the agency had relied on the approvals in several other decisions in a thirteen year period, concluding the agency's efforts to revise its approvals reflected "a clear change in policy." *Concerned Citizens of Bridesburg*, 836 F.2d at 786.

The case law provides agencies with narrow authority to reconsider and reverse previous decisions in the case of fraud or administrative mistake or error. In the 510(k) context, FDA would be allowed to nullify substantial equivalence determinations if fraud was used to obtain a substantial equivalence order, or the substantial equivalence determination reflected clerical or other administrative errors. The case law relied upon by the Working Group does not, however, permit the agency to nullify a 510(k) determination on substantive grounds.

III. RESCINDING ONE 510(K) CLEARANCE COULD RECLASSIFY AN ENTIRE GROUP OF DEVICES.

The 510(k) clearance process is a classification system based on predicate devices' classifications. Consequently, rescission of one 510(k) clearance would reclassify not only that device, but all devices that FDA determined to be substantially equivalent to it. This result would adversely affect all individuals whose rights to market such devices derive from a rescinded 510(k). In fact, the effect of a rescission on a predicate device, and all devices classified through reliance on the rescinded predicate, would be a reclassification into class III independent of the FD&C Act's reclassification authority, and a resulting PMA requirement before marketing. Permitting rescission would result in the denial of a statutory process that is intended not only to protect individual interests, but the public health.

Rescission of a 510(k) is unlike the withdrawal of a PMA, IDE, or PDP. These withdrawals are specifically authorized under the FD&C Act, and are product specific. Withdrawal of a PMA, IDE, or PDP only has direct regulatory consequences for a single product, and prior to a withdrawal becoming final, the FD&C Act prescribes protections

for the potentially affected party. In contrast, rescission of a predicate exceeds the interest of an individual and has potentially far reaching consequences, yet is unauthorized by the FD□C Act, and therefore, without protective processes to avoid governmental error or abuse.

Several concerns flow from the principle that rescission of a 510(k) is a reclassification action. First, as described below, assuming, arguendo, the existence of rescission authority, each potentially adversely affected person must be provided with adequate notice and an opportunity to participate in the rescission process. It is not enough for FDA to engage the 510(k) holder. Second, several express reclassification authorities exist under the FD□C Act. An effort by the agency to add a new one without a statutory basis warrants close scrutiny to ensure that FDA has not deviated from the legislative intent regarding device classification. Last, close scrutiny is warranted to ensure that the agency is not trying to circumvent use of its enforcement authority through the creation of an administrative substitute without adequate procedural protections.

IV. ASSUMING AUTHORITY TO RESCIND 510(K) CLASSIFICATION DETERMINATIONS, ANY RESCISSION REGULATION WOULD BE ACCOMPANIED BY AND INCLUDE SUBSTANTIAL PROCEDURAL PROTECTIONS AND RESOURCE BURDENS FOR FDA.

The 510(k) Working Group recommends that CDRH consider the procedures that would be necessary to rescind a 510(k). As stated above, the rescission of one 510(k) clearance would adversely affect all individuals whose right to market a device is derived from the rescinded 510(k). Any agency action with binding consequences for a group of individuals requires notice to all members of the group with an opportunity for comment. This is a basic principle of administrative law, *see* 5 U.S.C. □553, and inherent in the FD□C Act□s reclassification provision for preamendment devices and devices substantially equivalent to them, *see* □513(e) (requiring notice and comment rulemaking to reclassify devices to a lower classification).

If one assumes that FDA has the authority to rescind a 510(k), notice of the basis for the agency□s rescission cannot be limited to the 510(k) holder of record. FDA□s regulations require the agency to announce administrative action □of general or particular applicability and future effect□in the Federal Register. 21 C.F.R. □□10.3(a), 10.40(b). Further, to satisfy the Administrative Procedure Act and 21 C.F.R. Part 10, the notice must provide an adequate description of the bases for the agency action to allow meaningful comment by affected parties. 5 U.S.C. □553(b); 21 C.F.R. □10.40(b)(1)(vii). Thus, legally sufficient notice and the opportunity to comment must be provided to all individuals whose marketing clearance may be invalidated by a rescission.

In addition to notice and comment rulemaking, FDA must provide adequate procedural protections for each member of the class affected by the rescission. Because a substantial equivalence order permits marketing of a device based on the device□s classification,

issuance of the order effectively creates a property right that FDA has recognized in the context of persons selling their substantial equivalence orders and access to the agency file that supported the device's classification and clearance determination. *See* FDA, CDRH, *Device Advice, Device Regulation and Guidance: Medical Devices – Premarket Notification 510(k), at* http://www.fda.gov/MedicalDevices/DeviceRegulationand Guidance/GuidanceDocuments/ucm150086.htm (stating that "a 510(k) may be bought, sold, or transferred. FDA is not involved in transfers of ownership. The new owner should maintain information documenting the transfer of ownership of a 510(k), including any legal transactions that took place, in its 510(k) files.").

Before the agency may abrogate such rights, it must provide each potentially adversely affected party with adequate process for challenging the factual basis of a revocation, as applied to that party. *See e.g., Londoner v. Denver*, 210 U.S. 373 (1908) (requiring hearings for actions affecting identifiable individuals "who were exceptionally affected, in each case upon individual grounds").

The FD&C Act is consistent in defining the procedural rights of persons facing the loss of marketing rights, e.g., device and drug approvals. Specifically, when the agency undertakes to withdraw a device's PMA, the Act requires that the agency issue notice to the affected party and an opportunity for an informal hearing to challenge the proposed withdrawal order. Thereafter, if the PMA is withdrawn, the FD&C Act provides the affected person the option of an independent advisory committee review or a formal evidentiary hearing before an administrative law judge to challenge the agency's order to withdraw a PMA. In light of the strong protections afforded in other instances of agency revocation of marketing rights, the proposal's provision of only the right to an opportunity for an informal hearing is inadequate, and arbitrary and capricious. *See, e.g.*, *Teva Pharm. USA Inc. v. FDA*, 182 F.3d 1003 (D.C. Cir. 1999) (inconsistent treatment by the agency of similar situations is arbitrary and capricious).

Important protections afforded under Part 12 of FDA's regulations include a full evidentiary hearing, the right to cross-examine witnesses, an administrative law judge, and a greater opportunity to discover the agency's case than that provided in an informal hearing. These protections are critical to the accurate resolution of factual disputes such as those that would arise in the context of a proposed 510(k) rescission. All parties whose interests would be harmed because of factual and legal conclusions reached by the agency regarding a marketed class I or II device, *i.e.*, a predicate device, must have effective opportunities to contest the facts that underlie the proposed rescission.

Further, any regulation proposed by FDA regarding 510(k) rescission would be a "significant" regulatory action under an Executive Order governing regulatory planning and review, and would require review by the Office of Management and Budget's (OMB's) Office of Information and Regulatory Affairs (OIRA). Under Executive Order number 12866, as revised by Executive Order number 13258 and Executive Order number 13422, "[f]ederal agencies should promulgate only such regulations as are

required by law, are necessary to interpret law, or are made necessary by compelling public need.□ Exec. Order No. 12866, 58 Fed. Reg. 51,735, 51,735 (Oct. 4, 1993). This Executive Order requires agencies to annually provide OMB with a regulatory plan that includes a list of significant planned regulatory actions and the legal bases for such actions (e.g., □whether any aspect of the action is required by statute or court order□) for review by OIRA. *Id.* at 51,738. OIRA circulates each agency□s regulatory plan to regulatory policy advisors, for example, the OMB Director, and other agency heads. *Id.* at 51,738-39; Exec. Order no. 13258, 67 Fed. Reg. 9385, 9385 (Feb. 28, 2002). If any planned significant regulatory action conflicts with another agency□s policy or planned actions, is inconsistent with the priorities of the President of the United States, or is not required by law, necessary to interpret law, or made necessary by compelling public need, then the Director of OMB □may consult with the hea[d] of [the] agenc[y] with respect to [its] Plans, and, in appropriate instances, request further consideration . . . .□ Exec. Order no. 12866, 58 Fed. Reg. at 51,739; Exec. Order no. 13258, 67 Fed. Reg. at 9385.

The Executive Order defines significant regulatory actions as those that, among other things, may □[h]ave an annual effect on the economy of □100 million or more or adversely affect in a material way the economy, a sector of the economy, [or] . . . public health or safety.□ Exec. Order no. 12866, 58 Fed. Reg. at 51,738. Many types of devices that reach the market by means of a substantial equivalence order result in □100 million of business or more annually for manufacturers, distributors, and others in the health sector of the economy. Compound the value of the specific device by all substantially equivalent devices that could be affected by a rescission order and, even if the agency issues only a single rescission order in a year, the potential to exceed □100 million annually is likely.

The Executive Order also defines significant regulatory actions as those that □[r]aise novel legal or policy issues arising out of legal mandates, . . . or the principles set forth in this Executive [O]rder.□ *Id.* One principle enumerated in the Executive Order is that each agency □shall avoid regulations . . . that are inconsistent, incompatible or duplicative with its other regulations . . . .□ *Id.* at 51,736. As discussed below, rescission would duplicate, although without adequate protections, many of the enforcement authorities available to FDA under the FD□C Act, and of course, the FD□C Act□s reclassification provisions. Because 510(k) rescission is not authorized by the FD□C Act, and relates to a complex classification/marketing clearance question, any FDA regulation addressing or proposing rescission would be significant.

As amended, the Executive Order requires each agency to identify the □specific market failure . . . or other specific problem that it intends to address . . . that warrant new agency action, as well as assess the significance of [the] problem, to enable assessment of whether any new regulation is warranted.□ Exec. Order no. 13422, 72 Fed. Reg. 2763, 2763 (Jan. 23, 2007). As explained below, FDA does not need to rescind 510(k)s in order to protect the public health by removing predicate devices from use. As a result,

this new agency action could not be reasonably justified under the Executive Order. In light of yet another Executive Order requirement to assess the costs and benefits of the intended regulation, and . . . propose or adopt a regulation only upon a reasoned determination that the benefits of the intended regulation justify its costs a rescission regulation should not go forward. Exec. Order no. 12866, 58 Fed. Reg. at 51,736. As discussed above, the costs of rescinding a premarket notification could be quite substantial because not only would the rescinded 510(k) device be affected, but each and every device that claimed the device as a predicate would be affected.

In sum, a regulation establishing rescission of classification determinations would require substantial and costly procedural protections and compliance with Executive Order number 12866 (as amended) that would require that the cost of a rescission regulation be justified by a benefit, assuming authority exists to promulgate and enforce such a regulation. Because inappropriate predicates can be removed from use through administrative or judicial means at considerably less expense than a rescission proceeding that could implicate numerous devices and persons, a rescission regulation could not be reasonably justified in the context of the Executive Order.

V. FDA DOES NOT NEED TO RESCIND A 510(K) CLEARANCE TO PROTECT THE PUBLIC HEALTH.

Although the FD C Act does not provide FDA with the authority to rescind 510(k)s, it does provide several other means through which the government can remove an unsafe or violative product from the market, and thus, eliminate those products as predicates in the premarket notification process. FDA does not need 510(k) rescission to protect the public health.

For example, under the FD C Act, the government has express authority to remove devices from commercial distribution and use through the Act s injunction and seizure authority upon demonstrating, by a preponderance of evidence, that a device is adulterated or misbranded, *see* 332 334. The government can also effectively remove a device from the market through its replacement authority. *See* FD C Act 518(b). Moreover, the FD C Act provides FDA with very powerful administrative remedies to protect the public health, including mandatory recall authority, *see* 518(e) (authorizing a recall of any device that presents a reasonable probability of serious, adverse health consequences or death) and the authority to promulgate a regulation to ban a device, *see* 516 (if a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury and the manufacturer does not comply with the agency s request to correct or eliminate the risk through labeling).[1]

[1] Removal from the market of a device by FDA, and a judicial order of misbranding or adulteration, will result in the elimination of a predicate when the action would prohibit the re-introduction of the device into commerce. In other words, devices that can be reconditioned without new 510(k)s, e.g., if a device is enjoined from a distributor because of Good Manufacturing Practice (GMP) violations, once GMP-

The agency can use its express statutory authority under the FD□C Act to obtain a court□s determination of misbranding or adulteration, or device replacement order. These outcomes would eliminate devices from being predicates, *see id.* □513(i)(2), without the need for additional authorities. In other words, if there is something violative or dangerous about a specific device, the remedy is an action against the device or device owner and not against the □type of device□classified under section 510(k).

VI. THE GROUNDS PREVIOUSLY ASSERTED BY FDA FOR RESCISSION AUTHORITY DO NOT PROVIDE LEGITIMATE BASES TO RESCIND SUBSTANTIAL EQUIVALENCE ORDERS.

In a 2001 proposed rule, FDA asserted six grounds as bases to rescind 510(k) classification orders. *See* 66 Fed. Reg. 3523, 3524-25 (Jan. 16, 2001). None of these grounds necessitate the conclusion that a substantial equivalence order should be revoked. Several of the grounds previously relied upon by FDA permit a change in classification because the agency has altered its standards for making a substantial equivalence determination for a type of device. Other grounds for rescission asserted in the agency□s 2001 proposal are deficient because, even assuming their presence, it does not follow that rescission would be the appropriate remedy. In sum, none of these justifications in 2001 or now justify rescission.

VI. CONCLUSION.

FDA does not have express or implied statutory authority to rescind 510(k) classification determinations, nor are there compelling policy grounds to do so. We agree that FDA can nullify a substantial equivalence determination, if the 510(k) submitter procured the determination through fraud, or if the agency made an inadvertent administrative mistake or error and corrected it prior to the order becoming final. Rescinding one 510(k) clearance could potentially reclassify a group of devices, and FDA does not need to take such action in order to protect the public health. The FD□C Act provides the agency with numerous efficient means to remove unsafe or violative devices from the market, and eliminate them as predicates. Moreover, the FD□C Act authorizes FDA to reclassify devices based on new information, including reassessment of past information in the administrative record. The Working Group indicated that rescission would be seldom used in response to particular circumstances; we believe the law now provides adequate remedies for any such circumstance and fully provides adequate protection of the public health if the agency is willing to use the remedies Congress gave it to ensure safe and effective devices.

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compliant, the device is no longer adulterated and therefore could be marketed without any change to the device. Section 513(i)(2) is intended to eliminate predicates when the device cannot be re-introduced into commerce under its past clearance authority, *i.e.*, when modifications to the device to make it lawful would require a 510(k).

ATTACHMENT C

AdvaMed
Advanced Medical Technology Association

Proposal for Strengthening the 510(k) Process for a Subset of Medical Devices

The Premarket Notification 510(k) regulatory pathway ensures that diverse medical devices are appropriately regulated by creating a risk-based, science-driven classification system that *includes a comprehensive and vigorous review of device performance and test data.* A 510(k) submission for even simple devices may contain hundreds and in some cases thousands of pages of evidence demonstrating the safety and effectiveness of the device under review, including, where appropriate, clinical testing and data. By permitting incremental device improvements, today's 510(k) regulatory process is a successful and effective means to ensure the safety and effectiveness of medical technology while encouraging device development and facilitating the availability of high quality medical devices to meet the needs of the American public. Every year, approximately 3,600 new and improved devices are cleared via the 510(k) process – a remarkable record of achieving the twin goals of supporting medical innovation and providing the regulatory rigor necessary to assure that devices are safe and effective.

Challenges

Over the past two years, concerns have been raised regarding the adequacy of the 510(k) process to assure the safety and effectiveness of certain products that are cleared through the 510(k) regulatory pathway. AdvaMed believes much of this concern may arise from a lack of understanding among some stakeholders about the requirements of the 510(k) process and how it fits within the broader regulatory scheme including establishment registration and medical device listing, medical device reporting, good manufacturing practices as demonstrated by compliance with the quality system regulation, labeling requirements and provisions against adulteration and misbranding. This broad regulatory scheme assures that there is adequate FDA oversight and control throughout the medical device life-cycle.

FDA has also raised concerns, specifically regarding:

- The need for clinical information for some products when bench or animal testing are not adequate to provide assurance of safety and effectiveness or does not provide adequate understanding of the device
- The lack of access to final labeling copy prior to market introduction
- The lack of visibility to device changes that take place after marketing clearance including labeling and design changes that do not meet the criteria for a new 510(k) submission and
- The limits of postmarket controls.

More broadly, FDA has raised concerns about key aspects of reliance on predicates to determine the safety and effectiveness of new devices. For example, FDA has asked whether it is appropriate to clear a device based on the use of older predicates that no longer represent the standard of care and has raised concerns about the use of multiple or split predicates.

Current State

For the majority of Class II devices with low and moderate risk, or whose technical and clinical performance is well characterized, the current premarket notification requirements are adequate and appropriate, and provide FDA with the necessary information to conduct its substantial equivalence review.

For other devices whose intended use has the potential for increased concern or whose technology is being used in a new application, FDA has the authority to request any data necessary to assure the product is safe and effective. FDA also has the authority to require special controls. Special controls are information specific to a particular device type beyond the basic requirement of substantial equivalence that is considered important in the review of a device. Special controls can be applied to both the data that needs to be submitted for a device to be cleared for marketing beyond the basic requirement of substantial equivalence and to requirements relating to conditions of use. Special control documents have been developed for devices such as contact lenses, influenza assays, IV sets, sutures, and diagnostic ultrasound devices and transducers.

The 510(k) system works well for most devices, but in more complex submissions there appears to be a lack of clarity and consistency in the 510(k) review process. While there is no evidence to support that this has resulted in the clearance of unsafe or ineffective products, it has been a source of frustration and delay for manufacturers, especially new and small entities, trying to provide appropriate evidence to meet FDA requirements and has contributed to public concern about the process.

PROPOSAL

To meet FDA's mission of both protecting the public health *and* advancing the public health by speeding innovations that make devices safer and more effective, and to maintain the integrity of the 510(k) program, we recommend FDA establish requirements for additional information for a subset of Class II medical devices and *in vitro* diagnostics. Under the proposal, FDA would identify the device types subject to the enhanced information requirements and publish the list of affected device types in the Federal Register for public comment.

The list of device types to which the additional requirements apply would be reviewed periodically to add new device types where appropriate. Similarly, as more experience is gained and the use of a device becomes well-established with a historical track record of safe and effective use, the device would be removed from the list

Criteria for Identification of Class II Device Subset

The following criteria are recommended for determining which Class II devices should fall into a subset that would be subject to additional submission requirements. These criteria identify devices that may present a higher level of concern associated with their intended

use or with their use of technology in a new application. These devices clearly meet the requirements for Class II designation and do not meet the requirements for Class III.

Device types that may fall into this Class II subset could be the following:

- Permanent implants
- Life-sustaining
- Life-supporting

However, not all device types that are permanent implants, life sustaining, or life supporting would be subject to the additional submission requirements as many of these device types have a long history of safe and effective use and do not present added concern with their intended use. FDA would determine the subset of this group for which additional requirements are appropriate *based on risk management processes*. At a minimum, if the device type meets the following criteria, additional requirements would not be necessary:

- Well-characterized uses
- Well-characterized technologies
- A record of safety in clinical use or
- Up-to-date standards, guidance and/or special controls that have proven effective.

Some examples of these devices would be sutures and dental implants.

Enhanced Submission Requirements for the Class II Device Subset
510(k) submissions for Class II devices subject to the enhanced information requirements would include the following information:

- **Technical and Clinical Information Summary**
    - Technical Information
      Although bench testing and animal summary data are typically provided in a 510(k) submission, device specific testing may be appropriate for an identified device type (see Device-Specific Requirements *below*).

    - Clinical Information
      When animal and bench testing are not sufficient to provide an adequate characterization of the device, a summary of clinical information is provided. This includes relevant information about clinical experience with the device as well as experience with similar devices and the predicate device(s). Sources of clinical information may include:

        - Published and/or unpublished reports on other clinical experience of either the device in question or a justifiably comparable device

  - Results of pre- and postmarket clinical investigation(s) or other studies reported in the scientific literature of a justifiably comparable device
  - Results of pre- and postmarket clinical investigation(s) of the device

- **Labeling Elements –** Standard label information include indications for use, warnings and precautions and contra-indications.

Device-Specific Requirements – These device-specific requirements that FDA may require at its discretion for identified device types within this subset are in addition to the general enhanced submission requirements. These could include:

- Specification of additional evidence required to demonstrate safety and effectiveness, conformance to recognized standards, or other requirements related to the device types and

- A summary of manufacturing and controls information in the form of a flow chart or other simple means to establish baseline information to which subsequent 510(k) submissions and post-clearance periodic reports could be compared.

Instructions for Use at Time of Market Introduction for this Subset
Manufacturers of Class II devices subject to the enhanced information requirements would also be required to submit a copy of the device s final Instructions for Use at the time of first marketing of the device.

Post-clearance Periodic Reports for this Subset
Propose a system, that on a case by case basis, enables FDA to request at clearance, periodic reports for visibility to important changes to 510(k) baseline information and post-clearance experience after a device is marketed. Manufacturers of Class II devices subject to the enhanced information requirements *could* also provide to FDA Periodic Reports on marketed products every three years after the date of clearance that *could* include the information such as the following:

- **Design changes** [that do not meet the criteria for submission of a new 510(k)]

- **Labeling changes** [that do not meet the criteria for submission of a new 510(k)]

- **Summary of post-clearance experience** (e.g., MDRs; complaints; clinical information published within the reporting period) and

- **Update to the applicable device-specific requirements**

AdvaMed
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AdvaMed Proposal Responds to FDA concerns and Improves the Process
The current three-tiered classification structure of FDA device and diagnostic regulation is a risk-based approach. As such, it represents a practical and effective system for regulating an industry that is both very innovative and very diverse. The proposal effectively establishes a sub-tier of regulation for a limited subset of devices subject to 510(k), which could be accomplished without necessitating a statutory change. The additional requirements for this sub-tier add both transparency and consistency to the process for FDA and manufacturers while at the same time using the existing risk-based structure to increase the level of evidence associated with a targeted set of device types.

For the relevant subset of devices, this proposal assures that FDA has adequate clinical information needed when it makes clearance decisions, and allows FDA to specify in advance what additional information is necessary and appropriate to demonstrate safety and effectiveness. It assures that FDA has a copy of final labeling at time of market introduction, provides visibility for device and labeling changes that take place after market clearance, and provides FDA with additional postmarket data without burdening FDA with unnecessary documents or data.

With regard to concerns that reliance on predicates may not provide assurance of safety and effectiveness for some devices, the proposal addresses this issue directly by establishing specific evidence requirements for those categories of devices[1] where such requirements are necessary. Issues regarding use of outdated predicates, predicate creep, and use of multiple or split predicates all become irrelevant if there are specific evidentiary requirements that must be met regardless of the relationship of the new product to a predicate. As we have noted in AdvaMed s comments to the 510(k) review process docket, AdvaMed does not believe that FDA is required to clear any product based on any predicate without data providing satisfactory assurance to FDA that the new product is safe and effective. But the use of additional submission requirements (special controls) would clarify the evidence that manufacturers need to submit to gain product clearance, provide greater consistency in decision-making, and improve public confidence in FDA s decisions.

[1] To be clear, all 510(k) submissions include comprehensive information on the testing and performance of the device under review.

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COMPARISON OF ADVAMED AND CDRH 510(k) WORKING GROUP RECOMMENDATIONS
CLASS II SUBSET

PROPOSAL/ RECOMMENDATION	ADVAMED	CDRH WORKING GROUP	COMPARISON
Identification of a new subset ("Class IIb") for which more expansive data requirements will exist	Identification of ***small, focused, and dynamic subset*** of Class II devices subject to a sub-tier of regulation for which additional submission and postclearance requirements would apply to adequately evaluate the substantial equivalence of the device	Create "Class IIb," subset of Class II devices for which enhanced clinical information, manufacturing information, and/or additional postmarket evaluation would typically be necessary to support a substantial equivalence determination	AdvaMed's proposal does not contemplate and does not agree with the creation of a new class of devices ("Class IIb"). AdvaMed's proposal refers to a more limited and dynamic subset of Class II devices.
Statutory requirements re: new subset	Limited and fits within current classification scheme; does not require statutory change	FDA claims that creation of a new Class IIb is within the scope of the current, three-tiered device classification system established by statute	FDA may not have the statutory authority to create a Class IIb without new legislation.
Breadth of subset	Implantable, life-sustaining devices, and/or life-supporting devices; NOT included IF devices have well-characterized uses and technologies; a record of safety in clinical use; or up-to-date and effective standards, guidance, and/or special controls	Implantable, life-sustaining devices, and/or life-supporting devices (greater risk than other Class II devices); IVDs	Public FDA comments suggest Class IIb contemplated is more expansive than AdvaMed's proposed subset and could include all devices for which clinical data already are required (i.e., IVDs).
Identification of devices to include in subset	• Device types with higher level of concern associated with intended use or new technology using risk management processes; • FDA to publish list in Federal Register for comment; and • Once well-established with history	Aug. 31 Webinar: • Shuren: "... the establishment of Class IIb category is a mechanism by which we're looking to otherwise downclassify Class III devices."	The types of devices contemplated for enhanced requirements are similar, but public comment indicates that FDA's list likely would be more expansive and less subject to change over time.

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PROPOSAL/ RECOMMENDATION	ADVAMED	CDRH WORKING GROUP	COMPARISON
	of safe use, remove from list	• Includes IVDs	
Enhanced premarket requirements	• Device-specific technical bench testing • Clinical data (when animal and bench are insufficient), including published and/or unpublished reports of device or closely related device • Device-specific additional evidence of safety and effectiveness • Flow chart summary of manufacturing and controls	• Clinical data (least burdensome alternatives not discussed) • Manufacturing process and design control information • Aug. 31 webinar: The Agency recommended pre-IDE meetings to establish clinical study requirements for Class IIb devices.	As compared to the Working Group, AdvaMed's proposal contemplates alternative forms of clinical data, when necessary; device-specific nonclinical testing to support safety and effectiveness; and less extensive manufacturing information.
Post-clearance requirements	Post-clearance periodic reports (case-by-case) for design changes; labeling changes; postclearance experience; other updates	• Greater authorities to require postmarket surveillance/ condition-of-clearance studies • UDI system • Regular, periodic reports of modifications made without submission of a new 510(k)	AdvaMed did not propose enhanced postmarket surveillance or "condition-of-clearance" studies.
Labeling	Submission to FDA of final instructions for use at time of market introduction.	Regular, periodic updates to labeling. Labeling updates will be screened by FDA and posted to a public database.	AdvaMed did not propose placement of final labeling in a public FDA database.
Pre-clearance inspections	Not proposed	Proposed (with the intention of withholding clearance for noncompliance with QSR if potential for serious health risk)	AdvaMed did not propose withholding clearance or pre-clearance inspections.

ProXimal Ventures – Comment (posted 10/14/10)

FDA-2010-N-0348-0060

ProXimal Ventures
P.O. Box 255384
Sacramento, CA 95865
October 4, 2010

Comments on Docket No. FDA-2010-N-0348

Dear CDRH:

My investment firm ProXimal Ventures seeks to provide seed-stage funding to medical technology companies whose products address large markets and that can make healthcare safer, more effective, less costly, and more accessible, through technology. I am also involved as a volunteer in regional economic development efforts in support of dozens of such seed-stage companies. As a retired healthcare regulatory lawyer, I have some experience with agency-industry relations. As an American, I am concerned about our sluggish economic recovery, loss of manufacturing jobs, and the trend for early-stage medical device research and development to be sent overseas.

I have three general comments that address the FDA's role in medical device regulation that I believe would greatly enhance the ability for new innovation in medical technology to come to market where healthcare can be improved and made less costly, and where new industry can arise to rebuild our economy. Some may require statutory change, but I offer them in the spirit with which they have been solicited – in pursuit of a more effective and efficient regulatory process.

I also wish to thank Jeffrey Shuren and other FDA personnel who were at Stanford September 27-28 for their excellent program.

1. ***Small Innovative Trial Exemption.*** Persons subject to FDA medical device jurisdiction range from multi-billion dollar med tech companies, to minimally funded start-ups, researchers and inventors. Assertion of FDA jurisdiction over concept-stage and feasibility-stage prototype testing is of arguable public benefit and of such high cost that much of such early-stage testing is being driven overseas, or is dying due to lack of venture funding to support it. While it provides in theory an additional layer of protection to small patient populations, in practice it does nothing but stifle innovation. The FDA should exempt early-stage clinical trials involving fewer than (pick a number from 10 to 100) patients from FDA regulation entirely. Potential abuses and other harm to patients that might occur in such trials are adequately protected against by the professional integrity of physicians performing such testing, state licensing boards that supervise and discipline them, and by institutional review boards reviewing and approving such tests within institutions such as hospitals, plus they are by definition of very limited scale. FDA can publish whatever standards it expects to see in clinical trials that may ultimately be submitted to it in support of a PMA or "Class IIb" de novo 510(k) application, and early-stage product developers can follow these guidelines, once they've

perfected the prototypes they intend to go forward with, without having the FDA insert itself into the process of approving such trials through application for an IDE, in other than major trials. For most innovators and the angel investors who might support them, "getting FDA approval," even of just an IDE, is a major, complex and unknown process (subject to the added cloud that it is changing) that halts progress, or ends due diligence. Having an exemption for small-scale activity removes this major concern from the investment calculus. Although the data that results may not meet FDA standards, it may be sufficient to improve design, and attract the capital needed to move forward.

Justification. Such early stage innovative work hardly constitutes "interstate commerce," the potential harm is miniscule compared to the FDA's responsibilities with respect to devices being consumed in the millions or hundreds of thousands annually, and is adequately protected against at the state level and by local institutional review boards. Not having to deal with the FDA at all at the earliest stages of product development will add to efficiency in the innovation process. For every device for which clinical data is submitted to the FDA, there may be many device versions tested and improved before a final version is more fully tested, and there may be many devices or versions that are abandoned at this stage and never pursued. FDA involvement in all but those that go forward for major testing is wasted effort and an unnecessary burden on the innovators. The FDA should not seek to regulate this innovative stage. By exempting it, early-stage money will become much more available.

2. ***Adopt a Time-Limited "Provisional Approval" Process Based on Lesser Showings of Safety and Efficacy.*** FDA front-loads its regulatory burden, so that massive evidence of safety and efficacy may be required before the product can be introduced to market at all. The cost of meeting this burden can be in the neighborhood of $100 million. Yet most products that begin the route to approval never make it through to commercial success. It is now more common than not for such products to be tested in overseas markets and introduced in Europe before initiating FDA approval processes, a phenomenon almost entirely driven by regulatory burden. Venture capital funding for such new products is seriously constrained such that many promising new technologies have no way to move forward. VCs may require companies to pursue a foreign route. FDA should consider having a much lower burden in order to secure an initial "provisional approval" for a period of years, say five years, with potential one year extensions, perhaps subject to limited geographic area, such as a single state, during which time agreed-upon, more detailed clinical evidence can be compiled and published, and some degree of clinical experience independent of company-clinical trials can be generated. Perhaps limited geographic areas could also be approved, which would allow new products to prove themselves in a smaller market, while clinical dated is being accumulated.

Justification. More new products with great promise will become available in the US much earlier under provisional approval. The risk inherent in reduced initial clinical evidence required is mitigated by a limited time-frame during which provisional approval will be effective. At the time of final approval, both the Company and the FDA will have greater knowledge about clinical safety and efficacy, as well as unanticipated

developments from non-Company sponsored clinical use, to inform optimal approvals, indications for use, and conditions of use. Such reform would tend to halt the transfer of early stage design and development overseas. The amount of venture capital needed to get a new product to the stage where it can be acquired by a big company or go public will be greatly reduced, spurring greater activity. The medical community's role in filtering what devices should get used for what indications will occur on a parallel track with the agency's, rather than only after final agency action.

3. ***Redirect Limited FDA Resources from Pre-Market to Post-Market Supervision.*** The greatest harm to patients from defective medical devices occurs from high volume, implantable devices whose harmful effects become apparent only after lengthy implant experience, or from off-label use. FDA generally regulates devices after approval only due to reporting of problems, or very occasional audits. FDA should expand its supervision of post-market approval utilization of devices, to focus more of its limited resources on the areas of greatest potential harm, and reduce its focus on pre-market approval, by exempting concept-stage prototype testing, lowering initial provisional approval requirements, and negotiating post-market monitoring and supplemental clinical trial evidence requirements.

Justification. FDA's purpose is to protect the public from unsafe devices in the market, yet it functions instead as a gatekeeper to enter the market. This is similar to a police force trying to stop pickpockets in a marketplace by requiring all who would enter to prove that they are not pickpockets, while failing to assign any police to monitor the crowd. Every time a pocket gets picked, additional proof is required at the gate, stifling market activity. If instead, you put more cops in the market, and make it easier to get through the gate, you'll have a more robust yet safer market.

Very truly yours,

//s//
Cary M. Adams
Principal

Quintiles Consulting – Comment (posted 10/14/10)

Submitting on behalf of Quintiles Consulting, Medical Device Development Group

FDA-2010-N-0348-0061

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QUINTILES

October 4, 2010

Jeffrey Shuren, MD, JD
Director - Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue, WO66-5429
Silver Spring, MD 20993

Subject: Docket No. FDA-2010-N-0348 – Call for Public Comments

Dear Dr. Shuren:

On behalf of the Medical Device Development practice of Quintiles Consulting and our medical device clients, I am submitting these comments in response to FDA's notice in the Federal Register requesting public comment on these reports. Quintiles comments are in the attached table are limited to the "Foreword: A Message from the Center Director", and the "Center for Devices and Radiological Health 510(k) Working Group Preliminary Report and Recommendations". We fully support the proposed recommendations delineated in the "Task Force on the Utilization of Science in Regulatory Decision Making Preliminary Report and Recommendations".

Medical Device Development within Quintiles Consulting is regarded by many as the leading global regulatory consultancy for device development. The employees of our group have 57+ years experience as former FDA reviewers, supervisors, and managers at CDRH and 93+ years experience in device industry and/or as device consultants. Our experience extends across virtually all device types, including *in vitro* diagnostics and combination products, and across all points of the development continuum and all phases of the company life cycle, from start-up to established companies. Because of our 15+ year history with diverse device types, we have interacted with virtually every component of ODE and OIVD and thus have observed firsthand the emergence of varying practices and inconsistencies. In addition to Medical Device Development services, we provide our clients with seamless continuity supporting requirements for medical device quality systems, Good Clinical Practices, Good Laboratory Practices, and Process Optimization. We hold ourselves to extremely high standards of professionalism and are fully committed to advancement of FDA's public health mission.

Thank you for considering our comments. Quintiles Consulting remains dedicated to working with and supporting CDRH in the process of constructive change and would be pleased to provide additional clarification or information on these comments. Please feel free to contact me at 301-272-3113 or alternatively at david.west@quintiles.com.

Sincerely,

David West

David West, PhD, MPH
Vice President, Medical Device Development

Attachment I

Attachment I – Quintiles Comments on CDRH's Preliminary Internal Evaluations

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Page 1 – first paragraph: ". . . to advance three key objectives of a balanced public health approach: fostering medical device innovation, enhancing regulatory predictability, and improving patient safety."	Page 4, 1.1 Overview / Findings and Recommendations, 1st paragraph – "An effective 510(k) program is predicated on three major elements . . ."	Quintiles Consulting fully supports the three key objectives as stated, but urges CDRH to reaffirm the critical role of a "least burdensome" process in achieving these three objectives. The concept of "least burdensome" is to assure that the process requires only the scientific and technical information that is necessary and sufficient to demonstrate that a new device is substantially equivalent to a predicate device with respect to intended use and technological characteristics. The intent of "least burdensome" is not to undercut adequate science or patient safety, but to balance necessity with sufficiency in the current process. It would seem that this existing provision of law is being treated by the agency with increasing ambivalence in communications with the regulated industry and in actions regarding 510(k) submissions.
Page 1 – third paragraph: "By increasing the predictability, reliability, and efficiency of our regulatory pathways, we can help provide better treatments and diagnostics to patients more quickly . . ."	No specific text in Volume I	Increasing predictability, reliability, and efficiency of regulatory pathways, alone, will not provide better treatments and diagnostics to patients more quickly, nor stimulate investment in the development of promising new technologies, if the pathways are overly burdensome. Focus should be on determining what data are necessary and sufficient so that the regulatory pathways are optimized. Again, Quintiles Consulting urges CDRH to revitalize and reinforce the intent of "least burdensome" as provided by existing law.
Page 1 – fourth paragraph: ". . . FDA recently signed an information-sharing Memorandum of Understanding with the Centers for Medicare and Medicaid Services (CMS) . . ."	No specific text in Volume I	This type of inter-agency collaboration has the potential to speed the uptake of new device technology by facilitating CMS payment decisions on new devices. However, Quintiles Consulting recommends that the coordination between the two agencies should be approached with due regard to the differences in the respective missions and statutory authorities of the agencies and with due regard for safeguarding proprietary, confidential information.

Forward: a Message from the Center Director	**Volume I: 510(k) Working Group, Preliminary Report and Recommendations**	**Quintiles Comment**
Page 1 – fifth paragraph: ". . . to address critical challenges facing the Center and our external constituencies."	No specific text in Volume I	Quintiles Consulting seeks clarification of the Center Director's charge to the 510(k) Working Group with respect to addressing critical challenges. Did the 510(k) Working Group evaluate the adherence of staff and managers to established interpretation of existing laws, regulations, and policies? If not, Quintiles Consulting recommends that this evaluation be performed before implementing 510(k) program changes because we believe that addressing discrepancies in adherence could address some, if not many, of the problems encountered by the agency and industry. If this step of evaluating adherence was considered by the 510(k) Working Group but not pursued, Quintiles Consulting seeks clarification as to the rationale of the 510(k) Working Group.
No specific text in Volume I – Center Director comments focused on higher level objectives for a balanced public health approach, page 1	Page 3, 1. Executive Summary, 2nd paragraph – "The current 510(k) program reflects the current statutory framework and FDA's implementation of that framework through regulation, guidance and administrative practice.	Quintiles Consulting recommends that FDA consider a fourth major element of the 510(k) program as acknowledging and being sensitive to the incremental innovations and changes in new devices, as well as modifications of existing devices, in comparison to the predicate devices. Additionally, Quintiles Consulting believes that the review standard should reflect commonly understood and uniformly applied interpretation of prevailing laws, regulations, and policies, as well as understanding of the role of applicable regulatory practice and appropriate precedence. Transparency should prevail whenever law, regulations, policies, practices, or precedence are put aside or otherwise not followed. And lastly, Quintiles Consulting holds that the agency should require only "necessary" and "sufficient" information for making regulatory decisions.
Section I - Fostering Medical Device Innovation - Page 2, Item 1: "Streamline the premarket pathway for lower risk novel devices"	Page 5, 1.1 Overview / Findings and Recommendations, 1st complete paragraph – "Evaluation of Automatic Class III designation"	When the 510(k) *De Novo* program was initiated as part of the agency's implementation of FDAMA '97, the pathway was efficient and timely, with agency / sponsor pre-submission meetings leading to a common understanding of the suitability of the pathway and what information was to be placed in the 510(k) and the *De Novo* petition, respectively. Expectations were set with common adherence to statutory timeframes. However in recent times, ODE has discouraged pre-submission discussions on the suitability of the *De Novo* process for a device. Moreover, various branches within ODE approach the *De Novo* process with different understandings, and have indicated in informal conversations that the statutory timeframes for *De Novo* are viewed as unimportant.

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Page 2, Item 1: "Streamline the premarket pathway for lower risk novel devices", cont	Page 5, 1.1 Overview / Findings and Recommendations, 1st complete paragraph – "Evaluation of Automatic Class III designation", cont	Quintiles Consulting urges CDRH to revisit the agency practices that were in place when the program was first implemented and return to these practices, or provide clarification as to why these practices are no longer feasible. Quintiles Consulting has regrettably noted that FDA has been ambivalent in its treatment and management of the *De Novo* process. Quintiles Consulting maintains that *De Novo* process should be regarded as a legitimate pathway, when deemed appropriate by both FDA and the device company. Quintiles Consulting supports efforts to address inefficiencies in the current 510(k) *De Novo* process, as well as enhanced training of FDA personnel as to the value of this process and the value of open and earnest pre-submission discussions. The issue of requirements for clinical data should be considered independent of the issue of streamlining the *De Novo* process. Moreover, devices eligible for *De Novo*, under present statue, are devices for which there are no predicates. Thus, how could devices eligible for *De Novo* be presumed to be among certain types of devices placed in a subclass?
Page 2, Item 2: "Enhance science-based professional development for CDRH staff"	No specific text in Volume I but implicit in development of guidance and recommendations for training.	In addition to enhancing the science-based professional development for CDRH staff, Quintiles Consulting urges CDRH to include professional development with respect to existing laws, regulations, guidance, policy and practices. Oversight should not be restricted to adherence to good science, but also to adherence to applicable law, regulations, policies, practices and precedence. Thus, oversight should include holding the entire review staff (reviewers and managers) accountable for agency decision-making while adhering to good science, the law, regulations, policies, practices and precedence.

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Section II – Enhancing Regulatory Predictability - Page 3, Item 4 – "Increase the predictability of 510(k) data needs by establishing a new class IIb"	Page 5, 1.1 Overview / Findings and Recommendations, 3rd complete paragraph – ". . . develop guidance to define, as a heuristic, 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 . . ."	Quintiles Consulting believes that *a priori* requirements for clinical or manufacturing data will thwart innovation if not made commensurate with the degree of change of a new device from its predicate, or the degree of incremental change of a modification of an already cleared device. Rather than create a new classification, Quintiles Consulting recommends that CDRH re-examine and perhaps refine the 1986 Blue Book Memorandum guidance (#86-3) which established broad principles of when data should be required to support a 510(k), whether for a new device or for a modification of a device. Based on Quintiles Consulting experience in working with various Divisions and Branches within CDRH, we believe that some of the recent difficulties confronting the agency and the industry stem from inconsistent adherence to existing guidance. The industry encounters such inconsistencies from Branch to Branch within a Device Division, as well as across Divisions. This indicates a circumstance not driven by advanced technologies but driven by lack of CDRH training in a common philosophy and understanding of how the guidance should be applied. Quintiles Consulting firmly believes that re-consideration and revision of the 1986 guidance document, followed by CDRH-wide training, would be less disruptive for the agency and for industry than creating a new classification scheme outside the long-standing device classification paradigm established by existing statute.
	Page 6, 1.1 Overview / Findings and Recommendations, paragraph continued from page 5 – "By creating a "class IIb" device subset and making appropriate use of a streamlined de novo process, CDRH could make more predictable, timely, and consistent decisions."	The issue of requirements for clinical data should be considered independent of the issue of streamlining the *De Novo* process. Moreover, devices eligible for *De Novo*, under present statue, are devices for which there are no predicates. Thus, how could devices eligible for *De Novo*, having no predicates, be presumed to be among certain types of devices placed in a subclass?

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Page 3, Item 5 – "Notice to Industry" Letters	No specific text in Volume I	Although the existing process for guidance development may be time-consuming and to some extent cumbersome, it also provides a means for industry review and comment on draft guidance. Participation by industry and other affected constituents provides a safeguard against potentially ill-informed, impractical, or unfounded regulatory expectations being imposed on industry without adequate time for implementation or response. Quintiles Consulting agrees that a "fast track" method of providing industry with guidance would be welcomed, but recommends that the use of "Notice to Industry" letters include a feedback mechanism for industry or other affected constituents to provide comments to the agency before agency action on the guidance.
Page 4, Item 6 – "Clarify meaning of key terms in substantial equivalence . . ."	Page 4, 1.1 Overview / Findings and Recommendations, 3rd paragraph – ". . . key terms in the statutory definition of "substantial equivalence" have not been consistently interpreted by the Center . . .	Quintiles Consulting supports efforts to provide clarification and reinforce understanding of the statutory definition of "substantial equivalence" for FDA staff and for the medical device industry. Quintiles Consulting recommends FDA start this exercise from the last point in time at which the agency previously provided interpretation and guidance on defining substantial equivalence, which is FDA's Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3). Quintiles Consulting maintains that the inconsistent interpretation may be due to a lack of training and line management oversight to ensure that consistent interpretation is maintained. In our 15+ year history, Quintiles Consulting has observed that the significant inconsistencies in interpretation encountered are relatively recent phenomena. With the increasing numbers of experienced FDA employees retiring and new staff joining the agency, it would seem that these inconsistencies are more likely to be traceable to ineffective training and monitoring of training effectiveness with respect to consistent application of policy and/or guidance than due to advances in technology.

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
	Page 7, Item 1 Rational, Well-Defined, and Consistently Interpreted Review Standard, Same Intended Use: Lack of a Clear Distinction	"Intended Use" is a term used primarily in the context of making 510(k) regulatory decisions. "Indications for Use" or "Indications" are terms more readily recognized and understood by user healthcare professionals and patients when they appear in device labeling. Moreover, package insert labeling for drugs utilize the term "Indications and Usage", which is readily recognized by users, and is very close to the established device labeling term "Indications for Use". The agency should consider what confusion might arise among user healthcare professionals and patients who are accustomed to "Indications for Use" or "Indications". It seems that the agency should be able to address its internal problems of inconsistencies of interpretation and applying regulatory considerations for "Intended Use" though clearer guidance and better training, rather than forcing wholesale changes in terminology on itself, the industry, and users.
Page 4, Item 6 – "Clarify meaning of key terms in substantial equivalence . . .", cont	Page 7, Item 1, cont, Same Intended Use: Insufficient Guidance for 510(k) Staff and Industry	Law, regulations, and prevailing practice reflect that the product labeling and device design (explicit or implied) are established elements of a device application that should be considered in determining the "intended use" of a device. However, there is no basis in existing law or regulation to reflect that literature or existing preclinical or clinical data, in and of itself, would be a defensible basis for determining intended use. Moreover, trying to use literature or existing preclinical or clinical data as a basis for establishing intended use is likely to create potential for substantial and prolonged confusion, debate, and/or litigation.
	Page 8, Item 1, cont, Same Intended Use: Off-label Use	The approach of FDAMA '97 [Section 513(i)(1)(E)] and subsequent guidance *Determination of Intended Use for 510(k) Devices; Guidance for Industry and CDRH* Staff, January 30, 1998 (K98-1) would be a recommended starting point, perhaps with an analysis of shortcoming or limitations, if any, of that approach.
	Page 8, Item 1, cont, Different Questions of Safety and Effectiveness: Inconsistent Terminology	The 1986 guidance (#86-3) referred to "different TYPES of questions of safety and effectiveness" (emphasis added). This has served FDA and the industry well for decades and should be considered in any effort to reconcile or update the terminology and/or guidance.

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 5, 1.1 Overview / Findings and Recommendations, paragraph continued from page 4 – ". . . predicate comparisons . . . use of so-called "split predicates," a term that refers to using one predicate as the basis for a comparison with respect to "intended use" and another predicate as the basis for a comparison with respect to "technological characteristics" . . ..", and Page 9, Item 1, cont, Use of "Split Predicates" and "Multiple Predicates":	Quintiles Consulting believes two completely separate issues are being addressed here: (1) obsolete or ill-suited predicates and (2) "split predicates", and recommends that FDA address these issues separately. Quintiles Consulting recommends that the agency define specific criteria that would categorize a commercially available device as no longer eligible as a predicate device. When the agency deems that a particular predicate should no longer be considered as an eligible predicate device, FDA could notify manufacturers of this determination and the supporting rationale via the "Notice to Industry" mechanism or other means with timeliness of the process commensurate with public health urgency and opportunity for comment. Additionally, FDA could add a note to the 510(k) database to indicate the status as "not eligible as a predicate device", i.e., considered "misbranded". However, FDA would need to include provisions for distinguishing between a specific "misbranded" device from a more general type of device where the general type of device might remain suitable for continued commercial distribution.
No specific text in Forward	Multiple predicates / "split predicates", cont	Quintiles Consulting has understood that "split predicates" were not allowed simply on the grounds that matters of device design, performance, and labeling should be considered only within the context of the device intended use. That device design, performance, and labeling should be considered within the context of device intended use is grounded fundamentally in the law, and is reflected in numerous agency guidance documents stretching over years. Since "split predicates" were not allowed in the past, they should not be allowed now as there have been no changes to the law or guidance. If the use of "split predicates" has been allowed, Quintiles Consulting again believes this can be attributed to lack of training and managerial oversight of policy and practice. Quintiles Consulting recommends that the agency simply return to basic fundamentals of existing law and regulations in disallowing "split predicates" and also provide enhanced training of FDA personnel and industry to that effect, i.e., start with the intended use with the understanding that a new intended use creates a new device. Multiple predicates, all having a single, common intended use, should continue to be allowable to facilitate the review and marketing of innovative devices. If training is needed to clarify appropriate circumstances, then it should be undertaken.

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Page 4, Item 7 – Establish a Center Science Council . . ."	Page 6, 1.1 Overview / Findings and Recommendations, 2nd complete paragraph – " . . . in part through the oversight of a new Center Science Council comprised of experienced reviewers and managers, under the direction of the Deputy Center Director for Science."	Quintiles Consulting regrets that the current circumstances within CDRH are such that the formation of a separate Center Science Council appears to be the most suitable remedy to address inconsistencies in science-based decision-making. Traditionally, CDRH line managers would be held accountable to exert a level of internal oversight which would ensure sufficient scientific rigor and conformance with medical device law, regulations and policy. In the formation of this council to assure the quality and consistency of scientific decisions, Quintiles Consulting urges CDRH to also charge this council with assuring the consistency and conformance of decision-making with existing medical device law, regulations and policies. To achieve improvements in the current 510(k) program, decision-making must be consistent from a balanced perspective of both science and regulation.
No specific text in forward	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."	Oversight should not be restricted to adherence to good science, but also to adherence to applicable law, regulations, policies, practices and precedence. Thus, oversight should include holding the entire review staff (reviewers and managers) accountable for agency decision-making while adhering to good science, the law, regulations, policies, practices and precedence.

Forward: a Message from the Center Director	Volume I: 510(k) Working Group, Preliminary Report and Recommendations	Quintiles Comment
Section III – Improving Patient Safety - Page 4, Item 8 – "Require the up-front submission of more complete safety and effectiveness information to support the review of 510(k) devices"	Page 11, Item 2, cont, Quality of Submissions: Incomplete Information	Although this recommendation appears to be reasonable, in principle, it seems to extend the requirements for Class III summary and certification to all 510(k) devices, which would be to "provide a review of the risks and adverse events known and associated with the general category of devices into which the proposed device falls". Extending this requirement to all 510(k)s, which are submitted in great numbers per year, could result in workload burdens for the agency and industry. And because Class II devices frequently undergo numerous incremental changes, the value of the information is expected to be questionable and lead to frequent disagreements as to the relevance of the information to an iteration of a 510(k) device. Quintiles Consulting views this as over-reaching and believes that this requirement be limited to safety and effectiveness information immediately relevant to the device covered by the 510(k) and not to the prior versions of the device or to the claimed predicate device. For example, in FDA's "Guidance for Industry and FDA Staff - Format for Traditional and Abbreviated 510(k)s" , August 12, 2005, the agency recommends that sponsors "include a brief description of the device design requirements". This could be revised to recommend a description of device design requirements and identification of those design requirements that are essential for the safe and effective performance of the subject device. Some device-specific guidance documents recommend sponsors provide evidence of risk management activities, e.g., hazard analysis, design Failure Mode Effects Analysis (FMEA) human factors FMEA and/or process FMEA which capture safety and effectiveness issues immediately relevant to the device in question. CDRH could add this as a recommendation for all 510(k) devices.
Section III – Improving Patient Safety - Page 4, Item 8, cont	Page 11 - 12, Item 2, cont, Type and Level of Evidence Needed:	See previous comments; post-market Information: Substantial equivalence should be determined based on premarket data and analysis, and on confidence that the new device will perform as safely and as effectively as the predicate device. If the agency decides that a least burdensome approach would be to establish criteria under which substantial equivalence could be determined on a provisional basis, then the agency should provide means for safeguarding the clearances of devices found substantially equivalent to a device for which clearance is revoked for failure to fulfill "condition-of-clearance studies".

Forward: a Message from the Center Director	**Volume I: 510(k) Working Group, Preliminary Report and Recommendations**	**Quintiles Comment**
Page 5, Item 9 – "Create a searchable on-line public database to provide more detailed, up-to-date information to industry, the health care community and patients . . . one-stop source for detailed information . . . up-to-date labeling"	Page 14, Item 2, cont, 510(k) Databases:	In general, posting such information would appear to be helpful to users, patients, and the industry. However, present regulations require that 510(k)s include proposed labeling for the purpose of FDA determining the intended use of the device. Existing guidance allows for some changes to labeling without the need for submitting new 510(k)s, specifically FDA's "Deciding When to Submit a 510(k) for a Change to an Existing Device", January 10, 1997. Thus, any mechanism for posting "up-to-date device labeling" is expected to be overly burdensome for industry and FDA. An alternative would be to require manufacturers to post up-to-date labeling on their respective web sites, in which case it is publically available to users, patients, industry and the FDA. Limited Information on Current 510(k) Ownership: This used to be done, as a matter of custom, through "add to file" letters. Then FDA discouraged the practice and explained that the agency had no need or use for information on change of ownership. This raises the question of why the agency now believes it needs information on the change of ownership.
Page 5, Item 10 – "Clarify FDA's rescission authority . . ."	Page 8, Item 1, cont, Concerns about Predicate Quality and Rescission Authority	Quintiles Consulting appreciates the value of this recommendation. To be workable, Quintiles Consulting recommends that the regulation also must address how the rescinding of a 510(k) clearance would impact devices already cleared for marketing based on substantial equivalence to the device subject to the rescission. In other words, do the circumstances warranting the rescinding of a device apply equally to all devices found equivalent to the rescinded device before the rescinding action is taken? If this is the case, Quintiles Consulting urges the agency to consider how "due process" be assured for all parties. Perhaps CDRH should have a regulatory means, with timeliness of the process commensurate with public health urgency and opportunity for comment, to declare certain devices out of current clinical favor to be declared "misbranded" and thus not eligible for serving as a predicate. However, there should be provisions for distinguishing a specific "misbranded' device from a more general type of device where members of the general type of device might remain suitable for continued marketing.

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 10, Item 2 - Well-Informed Decision Making, Unreported Device Modifications	Revise guidance to clarify which modifications are allowable; this seems reasonable. It seems reasonable that the agency should have updated information. However, such updated information should already be available for agency review in design history files at company sites. If there is a requirement for periodic updates to be sent to CDRH, this will impose additional submission requirements on industry and obligate reviewers to review additional information not directly related to premarket review responsibilities. Review of the 510(k) "updates" is likely to fall to low review priority, similar to low review priority given from time to time for PMA annual reports and IDE annual reports If relegation to low priority occurs, the increased burden on both industry and the agency is not likely to yield the intended benefit. As an alternative, consideration should be given to issuing a guidance document on how updated information should be organized in design history files to facilitate review during routine or for-cause establishment inspections. If additional resources are available to FDA for a "510(k) update review responsibility", they could be more effectively placed in the field to undertake more frequent inspections (approaching biannual) focused on Design Controls, rather than at CDRH where they are likely to be siphoned off for uses other than reviewing routine 510(k) updates.

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 10 - 11, Item 2, cont, Quality of Submissions: Lack of Clarity	This proposal fails to recognize the critical interface between Design Controls and any premarket submission. Source data for product submissions such as rationales and supporting evidence should already be available in some form or another in design control documentation for the device. This should be true because FDA's Quality System Regulation, 21 CHR Part 820 requires it. A rigorous design control program should lead to ready identification of the necessary and sufficient information to fully support device safety and effectiveness or substantial equivalence. SMDA '90 authorized FDA jurisdiction over product development activities as a response to a high incident of design-related recalls. Title 21 Part 820.30 Design Controls has been in force since 1996 (the agency exercised enforcement discretion until 1997). However, inspections of medical device manufacturers do not routinely include the Design Control element, and in fact, FDA officials from ORA have publicly stated that FDA investigators tend to select other quality system elements to inspect with which they are more familiar. Thus, consideration should be given to a balance of oversight in requiring inspection of Design Controls on a routine basis and also providing guidance on how existing design control documentation should be compiled for a 510(k) submission. Introducing yet another new methodology such as an "assurance case" approach when there are two existing approaches where industry, reviewers and FDA investigators could benefit from re-training, would greatly improve the quality of documentation submitted, and also reduce duplication of effort. Such training should foster more ready agreements between agency reviewers and submitters on the design control documentation, as well as the necessary and sufficient subset of design control information to support marketing submissions. The authority to request photographs and/or diagrams, etc. already exist at 21 CFR 807.87 (e). The agency should simply inform the industry of its expectations. Such a requirement implies a requirement that a finished device be available prior to submitting a 510(k), which is not presently a requirement under existing law, Part 807, or Part 820. Moreover, a reviewer's visual inspection of a device ... as a basis for a regulatory decision ... might confound and prolong the writing of the agency record to support its regulatory decision.

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.

King & Spalding LLP – Comment (posted 10/14/10)

FDA-2010-N-0348-0062

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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 "G*uidance 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

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
			"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.

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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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			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.

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		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

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		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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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
• "[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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		and/or the device.	
• 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.	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.**	Current staffing levels, training, and knowledge management infrastructure limit Center-wide sharing of scientific knowledge and the development of new knowledge.		We support these proposals.
• Conduct an assessment of staffing needs to accomplish mission-critical functions.	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.	

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