

## **510(k) AND SCIENCE REPORT RECOMMENDATIONS: SUMMARY AND OVERVIEW OF COMMENTS AND NEXT STEPS**

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In August 2010, FDA's Center for Devices and Radiological Health (CDRH or the Center) released for public comment the preliminary reports from the 510(k) Working Group and the Task Force on the Utilization of Science in Regulatory Decision Making. These committees were established in September 2009 to address critical challenges facing the Center and our external constituencies. In recent years, concerns have been raised by all constituencies about how well the current 510(k) program was meeting its two public health goals of facilitating innovation and assuring that medical devices are safe and effective. In particular, industry had raised concerns that the 510(k) program had become less predictable, consistent and transparent thereby stifling innovation and sending companies and jobs overseas, and that CDRH reviewers had become less responsive and more risk averse. Consumers, third-party payers, and some healthcare professional groups were concerned that, for some devices, the 510(k) program did not provide adequate assurances of safety and effectiveness nor did it provide sufficient information for healthcare providers and patients to make well-informed treatment or diagnostic decisions. CDRH employees expressed concerns that the current 510(k) program failed to adapt to the increasing complexity of devices, and that reviewers' ability to make well-informed decisions was undermined by the poor quality of 510(k) submissions. In addition, an increasing workload was straining an already overburdened program.

The 510(k) Working Group was charged with evaluating how well the 510(k) program was meeting its two public health goals and exploring actions CDRH should take to strengthen it. In addition, the Institute of Medicine (IOM) is conducting an independent evaluation of the 510(k) program, and is expected to issue its report in mid-2011. The Task Force on the Utilization of Science was charged with making recommendations on how the Center can quickly incorporate new science — including evolving information, novel technologies, and new scientific methods — into its decision making in as predictable a manner as is practical. The overall objectives of the two CDRH reports are to foster medical device innovation and improve patient safety.

We have solicited and received a range of perspectives in developing the reports and on the recommendations contained in these reports at two public meetings and three town hall meetings, through three open public dockets and many meetings with individual stakeholders over the past several months. While there has not always been agreement on the best approaches for CDRH to take moving forward, there is widespread recognition that there is significant room for improvement. Seventy-six comments were submitted from medical device companies, representatives of the medical device industry, venture capitalists, healthcare professional organizations, third-party payers, patient and consumer advocacy groups, foreign regulatory bodies, trial lawyers, and others.

The comments reflected support, in some cases with a caveat or suggested modification, for the majority of the recommendations contained in both reports, especially those related to enhanced guidance and standard operating procedures (SOPs), greater transparency and clarification of review requirements, and increased training for Center staff and industry. Some recommendations received comments reflecting concerns from the majority of the constituencies represented. We have carefully analyzed and considered the comments received on all of the recommendations.

The Task Force and Working Group made a total of fifty-five recommendations addressing improvements to the 510(k) program and use of science and we received public comments on each of them. Twenty-eight of the recommendations received overall support from the comments submitted.

Twelve recommendations received support with a caveat or modification, and comments on the remaining fifteen expressed significant concern.

As we explain in Sections I and II below, over the next year we plan to implement or reach a major implementation milestone for the recommendations that received support or support with a caveat or modification. However, we will focus our efforts on making significant progress to implement those actions that will have the greatest impact on fostering medical device innovation, enhancing regulatory predictability, and improving patient safety. Those actions include streamlining the de novo process, issuing guidance to provide greater clarity about the 510(k) program, improving training for CDRH staff and industry, making greater use of external experts, and making critical business process improvements in CDRH, such as establishing a Center Science Council.

Given the comments received on seven of the recommendations, we recognize that implementing them may be problematic. Therefore, we will give the IOM an opportunity to provide feedback as part of its independent review of the 510(k) program before we make a final decision whether or not to implement some or all of these recommendations. Should the IOM offer comments we will take them into consideration. These recommendations, which are discussed in greater detail in Section III below, are as follows:

- CDRH should consolidate the terms “indication for use” and “intended use” into a single term, “intended use”;
- CDRH should expand its statutory authority to consider off-label use when determining the intended use of a device;
- CDRH should issue guidance on when a device should no longer be available for use as a predicate;
- CDRH should issue a regulation on its rescission authority;
- CDRH should require manufacturers to keep one unit of a device available;
- CDRH should issue guidance to create a “Class IIb”; and
- CDRH should seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices.

We intend to implement four of the recommendations about which there was significant concern only on a case-by-case basis through device-specific guidance. These recommendations, including other modifications made to them, are discussed in greater detail in Section III below. The original recommendations are as follows:

- CDRH should explore the feasibility of requiring manufacturers to provide regular, periodic updates of device modifications;
- CDRH should consider requiring 510(k) submitters to provide a list and brief description of all scientific information related to the safety and effectiveness of a new device known or reasonably known to the submitter;
- CDRH should issue guidance to clarify when manufacturing data should be submitted as part of a 510(k); and
- CDRH should clarify when it will withhold clearance for failure to comply with good manufacturing practices (i.e. when we will conduct a pre-clearance inspection).

We do not intend to implement the recommendation to eliminate the use of “split predicates”. As discussed in greater detail in Section III below, CDRH’s narrow use of the term “split predicate” is by definition inconsistent with the applicable provisions of the Food, Drug and Cosmetic Act. The concerns

expressed in the public comments regarding the use of split predicates appear to be more a matter of semantics than substance and, therefore, best addressed by no longer using the term “split predicate”. Instead, we will implement the recommendation to issue guidance to clarify the circumstances under which it is appropriate to use multiple predicates to demonstrate substantial equivalence, a practice we strongly support.

We intend to implement three additional recommendations about which there was significant concern. We have modified all of them in response to comments received. Our rationale for proceeding and a discussion of the modifications we intend to make are discussed in Section III below. The three recommendations included in this group - in their original and modified forms, as applicable - are as follows:

- **Original:** CDRH should create an online labeling repository.  
**Modified:** As in the case of prescription drugs, an online repository of medical device labeling can help inform clinical decision making. However, given the comments received on this recommendation, we believe it is important to seek additional stakeholder input at a public meeting before we take any steps to implement a scaled-back version of this recommendation to assure we proceed in a way that addresses the concerns raised in public comments and best meets the needs of stakeholders.
- **Original:** CDRH should adopt an assurance case framework for 510(k) submissions.  
**Modified:** We plan to implement an assurance case pilot program for infusion pumps, conduct an assessment of the pilot, and then seek public input before determining next steps to assure that we proceed in a way that addresses the concerns raised in public comments.
- **Original:** CDRH should create a public database of cleared devices that includes a photograph of each cleared device, to the extent they do not contain proprietary information.  
**Modified:** Given the comments received on this recommendation, we believe it is important to seek additional stakeholder input at a public meeting before we take any steps to implement this recommendation to assure we proceed in a way that avoids the disclosure of proprietary information and best meets the needs of sponsors and other stakeholders.

In total, we intend to implement these recommendations by taking twenty-five actions in 2011. These steps are set out in detail in our Plan of Action, which accompanies this Summary. The sections below contain a summary of comments received, a discussion of the areas of support or concern, a listing of the recommendations CDRH intends to implement, and those that will be referred to the IOM for feedback.

## I. Recommendations for which there was broad support

The recommendations that received strong support generally encouraged increasing the efficiency and transparency of the review process through guidance, enhancing training for CDRH staff and industry, assessing center staffing needs, and improving the quality of the review process and the use of new science by developing better internal business processes and engaging with external experts. CDRH intends to implement the recommendations from both reports that received strong support. They are:

Recommendation	Number
CDRH should 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.	4.1.1.1
CDRH should 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. 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.	4.1.1.1
CDRH should 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.	4.1.1.1
CDRH should continue ongoing efforts to develop better data sources, methods, and tools for collecting and analyzing meaningful postmarket information, consistent with the Center’s Strategic Priorities.	4.1.1.2
CDRH should conduct an assessment of its staffing needs to accomplish its mission-critical functions.	4.1.2
CDRH should continue the integration and knowledge management efforts that are currently underway as part of the Center’s Strategic Priorities.	4.1.2
CDRH should 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.	4.1.3
CDRH should 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.	4.2.1
CDRH should enhance its data sources, methods, and capabilities to support evidence synthesis and quantitative decision making as a long-term goal.	4.2.1
CDRH should continue its ongoing efforts to streamline its processes for developing guidance documents and regulation, consistent with its Strategic Priorities.	4.3.1
CDRH should develop and make public an SOP that describes the process the Center will take to determine the appropriate response to new scientific information, based on the conceptual framework outlined in Section 4.2.1. 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.	4.3.2

CDRH should develop or revise existing guidance to clearly identify the characteristics that should be included in the concept of “intended use.”	5.1.1.1
CDRH should provide training for reviewers and managers on how to determine “intended use.”	5.1.1.1
CDRH should develop and provide training for reviewers and managers on how to determine whether a 510(k) raises “different questions of safety and effectiveness.”	5.1.1.2
CDRH should 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.	5.1.2.3
CDRH should 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.	5.1.2.3
CDRH should provide additional guidance and training for submitters and review staff regarding the appropriate use of consensus standards, including proper documentation within a 510(k).	5.2.1.2
CDRH should develop and implement training for review staff and industry regarding the delineation between “class IIa” and “class IIb.”	5.2.1.3
CDRH should 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.”	5.2.1.3
CDRH should continue its ongoing effort to implement a unique device identification (UDI) system and consider, as part of this effort, the possibility of using “real-world” data (e.g., anonymized data on device use and outcomes pooled from electronic health record systems) as part of a premarket submission for future 510(k)s.	5.2.1.3
CDRH should develop guidance and 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.	5.2.2.1
CDRH should enhance existing staff training on the development and assignment of product codes.	5.2.2.1
CDRH should develop guidance and SOPs for the development of 510(k) summaries to assure they are accurate and include all required information identified in 21 CFR 807.92.	5.2.2.2
CDRH should develop guidance and regulations regarding appropriate documentation of transfers of 510(k) ownership.	5.2.2.2
CDRH should 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.	5.3.1.1
CDRH should consider establishing a Center Science Council comprised of experienced reviewers and managers and under the direction of the Deputy Center Director for Science.	5.3.1.1
CDRH should 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.	5.3.1.2
CDRH should develop metrics to continuously assess the quality, consistency, and effectiveness of the 510(k) program, and also to measure the effect of any actions taken to improve the program.	5.3.2

Several recommendations that received strong support will lead to greater innovation and enhanced regulatory predictability once implemented. Universal support was expressed for recommendations to enhance professional development and knowledge-sharing among Center staff, assure that appropriate scientific expertise and regulatory experience are brought to bear in decision making, and provide greater opportunities for Center staff to stay abreast of recent scientific developments and current clinical practice. Similarly, there was strong support for the development of a Center Science Council. Finally, recommendations to provide training for Center staff and industry on key terms related to 510(k) review and decision making and to provide greater clarity surrounding the timing and content requirements for clinical data submissions were met with strong support. However, because we are

delaying a final decision on creating a class IIb we will not develop and implement training regarding the delineation between class IIa and class IIb.

## II. Recommendations that received support, but with a caveat or suggested modification

The recommendations that received support with a caveat or conditioned upon modification generally address areas of the 510(k) process related to clarification of terms, increased access to information about marketed devices, or streamlining of processes that could be beneficial if implemented appropriately but, if not, could alter the review process or place greater burdens on manufacturers and/or CDRH. CDRH intends to implement these recommendations from both reports taking into consideration these caveats or modifications. They are:

Recommendation	Number
CDRH should 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.	4.1.1.1
CDRH should, consistent with its 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.	4.1.3
CDRH should 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.	4.3.1
CDRH should 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 the CDRH Transparency Website, the Center should move to release summaries of premarket review decisions it does not currently make public 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.	4.3.2
CDRH should reconcile the language in its 510(k) flowchart with the language provided in section 513(i) of the Federal Food, Drug, and Cosmetic Act (21 USC §360c(i)) regarding “different technological characteristics” and “different questions of safety and effectiveness.”	5.1.1.2
CDRH should 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 ( <i>e.g.</i> , a change in energy source, a different fundamental scientific technology).	5.1.1.2
CDRH should revise existing guidance to streamline the current implementation of the de novo classification process and clarify its evidentiary expectations for de novo requests.	5.1.3
CDRH should 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	5.2.1.1

modifications are eligible for a Special 510(k).	
CDRH should explore the possibility of requiring each 510(k) submitter to provide as part of its 510(k) detailed photographs and schematics of the device under review, in order allow review staff to develop a better understanding of the device’s key features.	5.2.1.2
CDRH should revise existing regulations to clarify the statutory listing requirements for the submission of labeling. CDRH should also explore the feasibility of requiring manufacturers to electronically submit final device labeling to FDA by the time of clearance or 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.	5.2.2.2
CDRH should 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.	5.3.1.2
CDRH should periodically audit 510(k) review decisions to assess adequacy, accuracy, and consistency.	5.3.2

The majority of comments on the recommendation to clarify the “least burdensome” provisions of the Act were from industry. Generally, comments noted that this is an important and useful provision, but it is often misapplied. We also received supportive comments from consumer and healthcare professional groups. Rather than revise current guidance, comments suggested that CDRH begin the clarification process by enhancing training for Center staff and industry on these provisions so as to ensure that they are appropriately applied and utilized. We agree with these comments and plan to provide additional training for Center staff and industry on the “least burdensome” provisions.

The recommendation to develop a network of external experts garnered support from industry and venture capital groups, although most comments questioned the use of social media to implement this recommendation. Comments from these groups encouraged the Center to draw upon experts from a wide variety of backgrounds and areas of expertise so as to leverage different points of view and bases of knowledge. Healthcare professional organizations generally supported this recommendation and were willing to serve as members of the network, but also were concerned about the use of social media in this context. Conversely, consumer groups expressed concerns about how CDRH could eliminate conflicts-of-interest when engaging external experts. We believe that our staff could benefit from leveraging external expertise to address scientific questions as long as the rules of engagement are appropriate and clear. We intend to develop an SOP that will outline in detail the parameters for Center staff engagement with external experts.

Comments from industry and some healthcare professional organizations on the recommendation to establish a process for issuing “Notice to Industry” letters were supportive of the increased transparency that such letters would provide, but were concerned that these kinds of letters would be used in place of guidance thus eliminating the opportunity for public comment the guidance process affords. Industry comments suggested that these concerns could be somewhat mitigated if there were an SOP for issuing “Notice to Industry” letters that clearly defined the parameters for when and about what topics the Center would issue such letters. In the interest of transparency, we plan to move forward with implementing this recommendation because the alternative is to continue to incorporate new science in our regulatory decision making in a nontransparent manner. However, consistent with comments received, we will implement a modified form of this recommendation by posting an SOP on our website that will clarify the parameters for issuing “Notice to Industry” letters when new scientific information changes our regulatory expectations.

We did not receive many comments on the recommendation to make more meaningful and up-to-date information available on our Transparency Website. The few comments we did receive on this

recommendation were from industry and consumer groups. Comments from industry expressed concerns about confidential or proprietary information being accessible on the internet. Comments from consumer groups were supportive of the increased access to information this recommendation would provide. As is set out in greater detail in our discussion of Recommendation 5.2.2.2 in Section III below, we do not intend to put confidential or proprietary information in this database. We intend to implement this recommendation because we believe increased transparency will help members of industry, patients, healthcare providers and CDRH staff.

Comments were generally supportive of the recommendations related to reconciling language in the 510(k) flowchart and the Food, Drug and Cosmetic Act (the Act) as long as changes to the approach used in the flowchart are not made, and clarifying the criteria for identifying “different questions of safety and effectiveness.” Most comments on the recommendation to reconcile the language in the flowchart and the Act were from industry. These comments noted that the flow chart reflects statutory language so any change would require notice and comment. Similarly, comments from industry and consumer groups mainly supported the recommendation to provide additional guidance to clarify the use and meaning of “different technological characteristics” and “different questions of safety and effectiveness.” We intend to move forward with implementing these recommendations by providing guidance to clarify key terms and ensuring that the terms in the flowchart are consistent with those in the Act.

Comments from industry, venture capital and patient groups were supportive of the recommendation to streamline the de novo process. Comments from some consumer groups indicated support for the recommendation, but cautioned that industry should not be allowed to manipulate the updated process as a loophole to avoid submitting a premarket approval application (PMA) for higher-risk devices. Other consumer groups felt that devices that are reviewed under the de novo process should instead be subject to a PMA. Third-party payers expressed similar concerns and urged CDRH to proceed carefully and make changes to the de novo process to ensure that only lower-risk devices are reviewed via that pathway. We believe that the de novo process, if used appropriately, can be an important pathway to market for lower-risk devices for which no predicates are available. We also appreciate the concerns raised by the comments on this recommendation and believe it is important to clearly delineate the eligibility criteria for the de novo process. Therefore, we intend to issue draft guidance to clarify and streamline the de novo process.

Most comments from industry expressed support for the recommendation to issue guidance clarifying what types of modifications do or do not warrant submission of a new 510(k). Members of industry that did not support this recommendation indicated that current guidance is adequate and this information is already reported to CDRH through other mechanisms. Some comments suggested that this recommendation, if implemented, be restricted to a subset of higher-risk devices. Although there is existing guidance on this topic, we find that some manufacturers are confused as to what types of modifications trigger the requirement for a new 510(k) submission. And, in some cases when a manufacturer did not submit a 510(k) for a modification that warranted submission, our current guidance did not adequately address those situations. Therefore, we intend to issue updated guidance to provide greater clarity as to the types of changes that would require submission of a new 510(k).

Comments from industry on the recommendation to require the submission of photographs or schematics concurred that such information can be helpful to a reviewer in making a determination of substantial equivalence. However, some comments objected to the idea that the submission of such information be an across the board requirement. Instead, some comments suggested that photographs or schematics be made available only for certain types of devices or only upon request. CDRH often receives detailed photographs and schematics as part of 510(k) submissions and our reviewers find such information helpful. Therefore, we believe that receiving photographs and/or schematics will improve

reviewer efficiency and effectiveness. We intend to issue guidance to clarify this requirement and outline the steps the Center will take to assure the confidentiality of these submissions.

Comments from industry were somewhat supportive of the recommendation to clarify statutory listing requirements for the submission of labeling, but some also expressed confusion over the recommendation. It was unclear to some commenters why, if CDRH has the authority to review labeling during inspections, industry should have to periodically submit labeling to the Center. Comments suggested that increased labeling requirements would place an undue burden on industry and CDRH due to the frequency of the reporting. Some comments suggested that annual reporting may be appropriate, but they did not support a requirement to submit an update every time a change is made. Others felt that this recommendation was redundant with efforts to develop a Unique Device Identification (UDI) system. We believe that periodically submitting updated labeling to CDRH would help the Center stay abreast of new information in product labeling and that periodically auditing the submitted labeling would aid the Center in assuring the quality and accuracy of device labeling. We disagree with the suggestion in the comments that we should use our inspection authority as the means to periodically obtain updated labeling, as we do not believe that would be a good use of the Center's resources. Moreover, such inspections would be disruptive for companies. To minimize the burden to all parties, CDRH will provide greater clarity on submitting a device's current labeling as part of the current requirement for manufacturers to submit updated listing information annually.

Comments from industry related to the recommendation on third-party review were supportive of continuing and improving the third-party review program, but cautioned against inappropriately limiting eligibility for third-party review. Comments from consumer and healthcare professional groups expressed concerns that third-party reviewers have potential conflicts-of-interest and consumer groups asserted that reviews should only be conducted by members of CDRH staff so as to ensure they are done correctly. We are supportive of the third-party review program and understand the concerns regarding conflicts-of-interest and inappropriately limiting device eligibility. Therefore, we plan to develop an SOP for updating our list of device types that are appropriate for third-party review to assure consistency and transparency in how we operate the program.

Finally, comments received on the recommendation to periodically audit 510(k) decisions were predominantly from industry. Although there was support for periodically auditing previous 510(k) decisions to assure quality and consistency in reviews, many comments voiced the concern that this process would be used to reverse previous decisions. Comments suggested that if this recommendation is implemented, the audit process should not be used to reverse previous 510(k) determinations for marketed products. We agree with these comments and believe they are consistent with the intent of this recommendation.

### III. Recommendations about which there were significant concerns

Significant concerns were raised regarding the following recommendations:

Recommendation	Number
CDRH should take steps to improve medical device labeling, and to develop an online labeling repository to allow the public to easily access this information.	4.3.1
CDRH should revise existing guidance to consolidate the concepts of “indication for use” and “intended use” into a single term, “intended use,” in order to reduce inconsistencies in their interpretation and application.	5.1.1.1
CDRH should explore the possibility of pursuing a statutory amendment to section 513(i)(1)(E) of the Federal Food, Drug, and Cosmetic Act (21 USC §360c(i)(1)(E)) that would provide the agency with 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.	5.1.1.1
CDRH should consider developing guidance on when a device should no longer be available for use as a predicate because of safety and/or effectiveness concerns.	5.1.2.1
CDRH should 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.	5.1.2.2
CDRH should 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.”	5.1.2.3
CDRH should explore the feasibility of requiring each manufacturer to provide regular, periodic updates to the Center listing any modifications made to its device without the submission of a new 510(k), and clearly explaining why each modification noted did not warrant a new 510(k).	5.2.1.1
CDRH should consider adopting the use of an “assurance case” framework for 510(k) submissions.	5.2.1.2
CDRH should explore the possibility of requiring each 510(k) submitter to keep at least one unit of the device under review available for CDRH to access upon request, so 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.	5.2.1.2
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.	5.2.1.2
CDRH should 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.	5.2.1.3
CDRH should 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.	5.2.1.3
CDRH should develop guidance to provide greater clarity regarding what situations may warrant the submission of manufacturing process information as part of a 510(k)	5.2.1.3
CDRH should 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	5.2.1.3
CDRH should 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.	5.2.2.2

CDRH has carefully considered all comments received on each of the recommendations listed above. Below, you will find a summary of the comments received on each of these recommendations and CDRH's plan of action (POA) for each recommendation.

➤ **4.3.1 - 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.**

We received comments on this recommendation from industry and consumer and healthcare professional groups. Comments from industry echoed their concerns about recommendation 5.2.2.2 below with regard to public access to confidential or proprietary information. Furthermore, industry comments asserted that device-specific labels are not necessarily appropriate for the general public, but rather are intended for physicians or other healthcare providers and may cause confusion if they are made available in a public database. Furthermore, the burden to disseminate labeling should rest solely with the manufacturer and should remain in the manufacturer's control. Additionally, comments from industry expressed concerns that this recommendation is an attempt by FDA to regulate commercial speech since many updates to labeling are for marketing purposes and not related to regulatory requirements or device alterations. Consumer and healthcare professional groups were supportive of this recommendation. They believe providing access to an online labeling repository would facilitate better-informed clinical decision making.

**POA:** We agree with comments that making labeling readily available could lead to better-informed clinical decision making. Just as the FDA's central repository for drug labeling conveys a public health benefit, we believe that a similar repository for devices would be of significant benefit to the public health by providing useful information to healthcare practitioners and patients. And, many manufacturers already post labeling on their website where it is publicly accessible. Moreover, annual submission of labels and certain other labeling for all devices is a current statutory requirement so there may be opportunities to create an online labeling repository with minimal burden on industry. However, we recognize there are challenges associated with developing a database of updated labeling and that there may not be value to practitioners and patients in making available the labeling for all devices or all parts of labeling, such as setup and installation guides. In addition, alternative approaches to an FDA labeling repository may be more practical, such as an FDA website that links to labeling that is housed on manufacturers' websites. Given the comments received on this recommendation, we believe it is important to seek additional stakeholder input at a public meeting before we take any steps to implement a scaled-back version of this recommendation to assure that we proceed in a way that addresses the concerns raised and best meets the needs of stakeholders.

➤ **5.1.1.1 - 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.***

We received comments on this recommendation from industry, venture capital, patient, consumer, healthcare professional and third-party payer groups. The comments generally expressed support for clarification and better definitions of these terms through guidance and training for Center staff and industry. However, industry and venture capital groups opposed the consolidation of terms because it could reduce current flexibility to include new indications for use under the same intended use, thus denying otherwise appropriate devices access to the 510(k) pathway. Moreover, it could have a chilling effect on innovation as manufacturers would have a disincentive to alter or improve their devices for fear of having to submit a PMA or pursue the de novo route for any new indication for use. Healthcare professional groups concurred and were concerned that these kinds of delays could impact the practice of medicine and patient care. Patient groups echoed these concerns while consumer and third-party payer groups were supportive of this recommendation.

**POA:** The intent of this recommendation was to reduce current confusion over the use of the terms “intended use” and “indications for use”; not to reduce the instances in which a new indication for use would still represent the same intended use. However, given the comments received, we understand that implementing this recommendation may not achieve our intended goal. Therefore, we will give the IOM an opportunity to provide feedback, after which we will consider all parties’ comments in reaching a final decision on whether or not to implement this recommendation.

- ***5.1.1.1 - The 510(k) Working Group recommends that CDRH explore the possibility of pursuing a statutory amendment to section 513(i)(E) of the FDCA that would provide the agency with express authority to consider an off-label use, under certain limited circumstances, when determining the “intended use” of a device under review through the 510(k) process. Such circumstances would include the availability of compelling evidence that the primary use of the marketed device will be off-label. If the Center were to pursue such an approach, it should also clearly define what type and level of evidence would be sufficient to determine that the off-label use is the primary intended use.***

We received comments on this recommendation from industry, venture capital, patient, healthcare professional and consumer groups. Industry and venture capital groups expressed concerns that this recommendation would place an undue burden on manufacturers. Specifically, comments noted that permitting the consideration of an off-label use could force industry to provide data on potential off-label uses even if the device under consideration was never intended to be used for such purposes. Other industry comments noted that a precautionary statement that the device has not been studied for off-label use may be sufficient to alert patients to the limitations of review. Some patient and healthcare professional groups expressed concerns that increasing CDRH’s authority to consider off-label uses would interfere with the practice of medicine and negatively affect patient care by hindering access to new technologies. Consumer groups were supportive of increasing CDRH’s authority to consider off-label use, but found the language of the recommendation too vague.

**POA:** Our recommendation was intended to be limited to the rare circumstance where a manufacturer seeks clearance for one use but actually intends to market the device for a different use in order to avoid having to provide data regarding the true intended use. In cases like this, the data provided in the 510(k) submission and CDRH’s decision to clear the device have nothing to do with the device’s true intended use and it is impossible for CDRH to conduct an appropriate review

or make an adequate determination of substantial equivalence. Thus, CDRH may end up clearing a device for a use for which it has not reviewed any relevant data. However, given the comments received, and the challenges of drafting new legislative authority narrowly tailored to these limited circumstances, we understand it may not be feasible to implement this recommendation without inadvertently restricting the practice of medicine. Therefore, we will give the IOM an opportunity to provide feedback, after which we will consider all parties' comments in reaching a final decision on whether or not to implement this recommendation.

- ***5.1.2.1 - 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.***

We received comments on this recommendation from industry, healthcare professional, patient and consumer groups. Industry comments noted that section 513(i)(2) of the Act governs the types of predicates that are inappropriate for use in determining substantial equivalence. They suggested that this recommendation would require a statutory amendment to be enacted, as it would lower the threshold already established under the Act for disallowing predicates. In addition to this argument, comments from industry and patient groups indicated that disallowing the use of certain devices as predicates would limit the number of available predicates and would therefore limit the availability of the 510(k) pathway for otherwise eligible devices. This would lead to longer review times for many devices that would otherwise be cleared more rapidly through the 510(k) process. Many industry comments also questioned what would happen to marketed products that had used the disallowed predicates in their 510(k) submissions. Comments from some industry members acknowledged that some predicate devices are substandard and disallowing their use as predicates might improve the overall safety and effectiveness of medical devices. Comments from some healthcare professional organizations concurred, noting that CDRH should track the safety and effectiveness of predicate devices and should require safety and effectiveness data for any new devices using predicates that have received significant adverse event reports. Consumer groups supported this recommendation and agreed that allowing a substandard device to be used as a predicate raised patient safety concerns.

**POA:** We remain concerned that allowing a device to be used as a predicate after it has been removed from the market due to safety problems would place patients at risk because the newer device may present the same risks as the predicate device. However, given the comments received, we understand that implementing this recommendation may have unintended consequences. We also note that, in appropriate circumstances, we may be able to rescind a 510(k) for a device that the manufacturer has recalled and then decided to withdraw from the market altogether due to significant safety problems, thereby removing its availability for use as a predicate; an approach that could be applied on a case-by-case basis. Therefore, we will give the IOM an opportunity to provide feedback, after which we will consider all parties' comments in reaching a final decision on whether or not to implement this recommendation.

- ***5.1.2.2 - 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.***

We received comments on this recommendation from industry, consumer, healthcare professional and third-party payer groups, and trial lawyers. Some industry comments questioned CDRH's authority to rescind a 510(k) clearance. Others noted that CDRH already has the authority to rescind a 510(k) clearance under certain circumstances in addition to the ability to recall devices and issue warning letters, so expanding this authority would be unnecessary and duplicative. Many industry and some healthcare professional group comments also called for clarification and guidance on what would happen to marketed devices that had used a device as a predicate for which the 510(k) clearance was rescinded. Comments from consumer, third-party payer and some healthcare professional groups and trial lawyers were supportive of expanding CDRH's authority to rescind a 510(k) clearance. Other healthcare professional groups were supportive of the application of CDRH's rescission authority in limited circumstances.

**POA:** We agree that we have the authority to rescind a 510(k) clearance under appropriate circumstances. This recommendation was intended to provide clarity through rulemaking as to the scope of our current rescission authority. However, given the comments received, we are delaying a final decision on rulemaking related to this recommendation to give the IOM an opportunity to provide feedback. With regard to an appeals process for rescission decisions, we will address that issue through guidance on appealing CDRH decisions, which is already in development as part of the Center's 2011 Strategic Priorities.

- ***5.1.2.3 - 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, the Center should update its existing bundling guidance to clarify the distinction between multi-parameter or multiplex devices and bundled submissions.***

We received comments on this recommendation from industry, venture capital, consumer, healthcare professional and third-party payer groups, and trial lawyers. Overall, while comments from industry and healthcare professional groups generally supported providing greater clarity on the use of multiple predicates, they raised the concern that disallowing split predicates would prevent certain otherwise appropriate devices from being eligible for review via the 510(k) pathway, thus increasing the number of de novo or PMA applications. Venture capital associations echoed this concern adding that it could stifle innovation. Many industry and healthcare professional comments argued that newer technologies are more likely to use split predicates; therefore, eliminating their use would stifle innovation. Some industry comments agreed that the use of split predicates may be inappropriate in some circumstances and CDRH could address the issues created by the use of split predicates through stricter guidance and asking industry to justify when the use of split predicates is appropriate. In addition, some industry comments noted that the use of multiple predicates is different than the use of split predicates and multiple predicates should be allowed regardless of CDRH's determination regarding split predicates. Some consumer and third-party payer groups and trial lawyers were supportive of eliminating the use of split predicates to increase patient safety.

**POA:** CDRH strongly supports the use of multiple predicates. However, a true split predicate refers to a situation in which a 510(k) submitter is attempting to "split" the 510(k) decision making process by demonstrating that a new device has the same "intended use" as one predicate while comparing the new device's "technological characteristics" with a second predicate that has a different intended use. For example, in the case of a 510(k) submission for a new microscope-aimed, computer-controlled laser pipette, the submitter could not cite a standard mechanical pipette for intended use and a medical laser for technological characteristics to achieve a substantially

equivalent determination because the new device raises different types of questions of safety and effectiveness. A determination of substantial equivalence in this case would be inconsistent with the 510(k) standard. Requests to use true split predicates are rare, affecting less than 1% of 510(k) submissions.

A new device that possesses new technological characteristics (such as a novel material) may be found to be substantially equivalent to a predicate device with the same intended use but different technological characteristics as long as the technological characteristics of the new device do not raise different types of questions of safety and effectiveness. For this to be the case, scientific methods must be available to assess the effects of the new technological characteristics, and performance data must be available that demonstrates substantial equivalence. In this example, if the submission for the new device compared intended use and technological characteristics with the first predicate and cited a second predicate that used the novel material in the same anatomical location for approximately the same duration as the new device, the second predicate could be used to show that the novel material as used in the new device does not raise different questions of safety and effectiveness regarding the material's properties or performance. This is an example of multiple predicates and is not considered a split predicate by CDRH.

Given the comments received on this recommendation, it is clear that the term "split predicate" means different things to different groups. For CDRH, the use of a true split predicate is, by definition, inconsistent with the 510(k) regulatory standard. Therefore, we believe the better approach in this case would be to no longer use the term "split predicate". Instead, we will issue guidance to clarify the circumstances under which it is appropriate to use multiple predicates to demonstrate substantial equivalence.

- ***5.2.1.1 - 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).***

We received comments on this recommendation from industry and consumer and third-party payer groups. Most industry comments stated that FDA has the authority to inspect manufacturers to obtain this information at any time, so additional reporting is unnecessary. Furthermore, whenever manufacturers submit a new 510(k) for an updated device, a record of all changes made is required to be submitted. Thus, CDRH already receives modification updates through this mechanism. Comments noted that manufacturers make many insignificant changes to devices on a regular basis. Given the large volume of modifications, industry comments questioned CDRH's ability to handle the number of submissions the Center would receive in response to this recommendation. Comments suggested that, if CDRH chooses to implement this recommendation, it be restricted to specifically identified types of modifications so as to reduce the burden on industry and the Center. Consumer and third-party payer groups were supportive of this recommendation.

**POA:** It is true that a manufacturer must include all prior unreported modifications as part of a new 510(k) submission when the manufacturer makes a modification that triggers the requirement for a new 510(k) submission. However, we continue to find instances in which manufacturers make changes that warrant a new 510(k) submission, but treat those changes as unreportable. Because new 510(k)s may be submitted years after unreported modifications are made, if at all, we cannot rely on them as the sole source for modification information. Furthermore, conducting inspections to gather this information would not be practical or effective, and would be unnecessarily disruptive

to manufacturers. We do recognize that submitting all modifications for all devices could be overly burdensome for us and manufacturers, and might not be necessary to assure that new 510(k)s are submitted when appropriate for modifications to cleared devices. Generally, the circumstances under which it would be most helpful to receive periodic reports of modifications are when a change is made to a higher-risk device for which the impact on safety or effectiveness is unclear; specifically, it is unclear whether or not CDRH should require the submission of a 510(k). In these cases CDRH would want to be notified periodically that such a change was made in lieu of submitting a 510(k). Because these circumstances are very device-specific, we will implement this recommendation only on a case-by-case basis through device-specific guidance.

- ***5.2.1.2 - 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.***

We received comments on this recommendation from industry and third-party payer groups. The majority of industry comments noted that the assurance case framework may be appropriate when applied to certain types of higher-risk devices, but they objected to the widespread application of this framework for all device types. Other industry comments noted that use of an assurance case framework may cause confusion since many manufacturers are unfamiliar with this concept and it would require extensive reviewer training, which may hinder the already overburdened review process. Comments from third-party payers were generally supportive of the assurance case framework and enhancing CDRH’s ability to link claims to evidence.

- ***POA:*** We believe the use of assurance cases can improve the review of 510(k) submissions while assisting sponsors in identifying potential weaknesses in their 510(k)s prior to submitting them to CDRH. Our recent experience with using the assurance case approach for infusion pump 510(k) submissions supports this conclusion. For example, some manufacturers have found the approach helpful in identifying inadequately mitigated risks thereby allowing them to resolve those issues before submitting a 510(k), thus facilitating a timely review of their submissions. Therefore, we intend to implement a modified version of this recommendation. Specifically, we will begin a pilot program to study the use of an assurance case framework for infusion pumps. We will make an assessment of the pilot program available to the public upon the program’s completion and seek public input before deciding whether or not to apply an assurance case approach to other device types and, if so, which ones.
- ***5.2.1.2 - The 510(k) Working Group further recommends that 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.***

We received comments on this recommendation from industry and healthcare professional groups. Industry raised concerns that storing device prototypes would be overly burdensome and it is often difficult to install or calibrate larger devices. Also, comments pointed out that many manufacturers do not begin manufacturing a device until after they receive 510(k) clearance, so requiring a device prototype as part of an application could force manufacturers to incur costs when they do not know if the device will be cleared for marketing. Most comments indicated a willingness to provide a prototype upon request, but did not believe that such a requirement should be mandatory. Healthcare professional groups were in support of this recommendation.

**POA:** Given the comments received, we recognize that keeping one unit of a device available may be overly burdensome to industry. Therefore, we will give the IOM an opportunity to provide feedback, after which we will consider all parties' comments in reaching a final decision on whether or not to implement this recommendation.

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

We received comments on this recommendation from industry and healthcare professional, consumer and third-party payer groups. Comments from industry asserted that this recommendation would place an undue burden on manufacturers and would make the 510(k) process more like that for a PMA because manufacturers would have to conduct an exhaustively broad search yielding large volumes of information to satisfy this requirement. Comments also questioned CDRH's ability to analyze the amount of scientific information that would be provided if 21 CFR 807.87 were amended as the recommendation suggests. Some comments expressed support for a version of this recommendation that is narrower in scope. Consumer, some healthcare professional, and third-party payer groups expressed support for this recommendation.

**POA:** Given the comments received, we recognize that this recommendation may be too broad in scope and overly burdensome, particularly if it includes information that "should be reasonably known" to the submitter. Although we believe that submitting a brief description of scientific safety and effectiveness information for at least a subset of devices, such as higher-risk and novel technologies, would improve the quality of CDRH decisions and help review staff minimize the need to request additional information from sponsors, the circumstances under which submitting such information may be appropriate are device-specific. Therefore, we will implement this recommendation only on a case-by-case basis through device-specific guidance. And, in these cases, we will limit submissions to a brief description of safety and effectiveness information specific to the device to be reviewed that is *already known* to the submitter. Limiting the submission to information already known (rather than known or reasonably known) should not be burdensome because such information should have been reviewed as part of sponsors' due diligence in preparing their 510(k) submissions.

- **5.2.1.3 - 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. Delineating between "class IIa" and "class IIb" would not reconfigure the current, three-tiered device classification system established by statute; it would represent only an administrative distinction. The development of**

***a “class IIb” guidance would provide greater clarity regarding what submitters would generally be expected to provide for certain 510(k)s. Determining what device types might be included in “class IIb” would require further consideration. Potential candidates may include some implantable, life-sustaining devices, and/or life-supporting devices, which present greater risks than other class II device types. A specific type of device may be removed from the “class IIb” subset as its technology and its risk/benefit profile in clinical practice become better understood. The types of evidence that could be required for “class IIb” devices are discussed in greater detail in the following subsections. As part of its guidance, CDRH should make clear that the delineation between “class IIa” and “class IIb” is meant to be a general guideline only. The types of evidence described below may at times be required for a device that was previously in “class IIa” but for which the Center has changed its evidentiary expectations on the basis of new scientific information, as described in the preliminary report of the Task Force on the Utilization of Science in Regulatory Decision Making. In addition, such evidence may be required for a device that has not yet been specifically identified as a “class IIa” or “class IIb” device. For example, in some situations, a new device may be developed whose technology or use may be so new that it is not possible for CDRH to determine whether it should be included in “class IIa” or “class IIb” until it meets with the submitter to obtain more information. Further, it is possible that not all devices within the “class IIb” subset would necessarily require all of the types of evidence described below; therefore, the guidance should advise manufacturers of “class IIb” devices to engage with the Center to discuss the type of evidence appropriate for their devices.***

We received comments on this recommendation from industry and consumer, patient, healthcare professional, and third-party payer groups, trial lawyers, and foreign regulatory bodies. Some comments received from industry asserted that Class IIb would constitute an additional class, not a sub-class, and CDRH does not have the statutory authority to create an additional class. Other comments from industry were supportive of creating a sub-class for a small group of higher-risk devices if guidance is provided for such devices. In addition, they suggested that higher-risk devices can be managed through the use of special controls. Industry comments cautioned that there would likely be confusion surrounding which devices should be categorized as Class IIb versus Class III and subject to PMA requirements. Many industry comments urged CDRH to consider a case-by-case analysis of higher-risk devices to determine which devices would require additional clinical data rather than creating a separate sub-class. Other industry comments indicated that creating a subclass to assist manufacturers in determining the level of clinical evidence necessary to demonstrate substantial equivalence would be helpful. Comments from some healthcare professional organizations also opposed the creation of a Class IIb for the reasons stated above. Comments from patient groups cautioned that what they perceived to be increasing scrutiny of devices that would otherwise be cleared under 510(k) would inhibit patient access to new devices. Consumer groups were supportive of the increased level of scrutiny that they believe the creation of Class IIb would provide for review of the devices in that class, but some consumer groups expressed concerns about including implantable, life-supporting or life-sustaining devices in the new Class IIb subset because they thought these devices should be subject to a PMA. Similarly, some third-party payer groups were concerned that higher-risk devices that should be classified as Class III will end up in Class IIb and will not be subject to the level of review that should be required for such devices. Other third-party payer groups were pleased that Class IIb would enable what they view as a stricter review standard for certain higher-risk devices and enhanced patient safety. Foreign regulatory bodies were supportive of the creation of a Class IIb because it would bring U.S. regulations closer to those of the European Union. Trial lawyers were also supportive of the creation of a Class IIb because they believe it will improve the safety of 510(k) devices.

**POA:** The intent of this recommendation was not to expand the types of devices subject to clinical data requirements, but rather to place a greater onus on CDRH to identify in advance those devices for which clinical data would be required. However, given the comments received, we understand that implementing this recommendation may have unintended consequences. Therefore, we will give the IOM an opportunity to provide feedback, after which we will consider all parties' comments in reaching a final decision on whether or not to implement this recommendation.

- **5.2.1.3 - 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.**

We received comments on this recommendation from industry, consumer, healthcare professional and third-party payer groups, trial lawyers and foreign regulatory bodies. Comments from industry and some healthcare professional groups noted that CDRH already has the authority to require postmarket studies by using special controls, and has the Medical Device Reporting and MedSun programs, so this requirement is unnecessary. Some comments from industry suggested that postmarket surveillance would be overly burdensome and could stifle innovation. Other comments from industry acknowledged that condition of clearance studies may be appropriate for certain types of higher-risk devices. Other comments from healthcare professional groups noted that additional postmarket surveillance requirements could place a greater administrative burden on physicians, which would interfere with patient care and access to doctors. Consumer and third-party payer groups, trial lawyers and foreign regulatory bodies were supportive of granting FDA the authority to require condition of clearance studies. Of note, FDA has the authority to order postmarket surveillance as a condition of clearance but it is limited to Class II or III devices that are intended to be used in pediatric populations.

**POA:** Given the extent of the concerns raised, we will give the IOM an opportunity to provide feedback on this recommendation, after which we will consider all parties' comments in reaching a final decision on whether or not to implement this recommendation.

- **5.2.1.3 - 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).**

We received comments on this recommendation from industry. Comments stated that this recommendation would place an undue burden on both industry and the Center with little benefit. In addition, comments expressed concern that many manufacturers do not have manufacturing information available at the time an application is submitted since they do not intend to put a device into production unless it receives 510(k) clearance. Comments suggested that, if CDRH implements this recommendation, it should be restricted to certain classes of higher-risk devices and that CDRH provide guidance highlighting the type and scope of information required.

**POA:** CDRH already requests manufacturing information for some devices, but we have not provided clarity for sponsors as to when we would request such information. In addition, we agree that manufacturing process information should be provided only for a subset of higher-risk devices for which the receipt and review of such information could prevent potential safety or quality problems. Because the circumstances under which submitting such information may be appropriate are

device-specific, we will implement this recommendation only on a case-by-case basis through device-specific guidance. Such guidance would describe the type(s) of manufacturing information requested, which would be tailored to address relevant issues specific to that type of device.

- **5.2.1.3 - 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.**

We received comments on this recommendation from industry, consumer and third-party payer groups, and foreign regulatory bodies. Comments from industry objected to withholding clearance on the basis of pre-clearance inspections. They asserted that a determination of substantial equivalence does not have any relationship to compliance with current Good Manufacturing Practices. Industry comments expressed concern that pre-clearance inspections would delay bringing a product to market and that CDRH lacks the resources to perform these inspections in a timely manner. Comments from industry also expressed doubt that CDRH would derive any benefit from conducting these kinds of inspections. Finally, some industry comments also voiced concerns related to the need to have manufacturing systems in place prior to receiving 510(k) clearance. Some members of industry expressed support for this recommendation if it were restricted to the types of devices for which failure to comply with cGMP would pose a significant risk to human health. Consumer and third-party payer groups and foreign regulatory bodies were supportive of CDRH conducting pre-clearance inspections.

**POA:** We currently have statutory authority to withhold clearance until we have conducted pre-clearance inspections in certain limited circumstances. From time to time, we use this authority, but we have not clarified under what circumstances we would use our existing authority. We do believe it would be helpful to sponsors and to CDRH personnel to clarify when we would exercise our authority to conduct a pre-clearance inspection and thereby provide greater predictability, consistency, and transparency. In addition, we agree that when a pre-clearance inspection is warranted, it may not be feasible or appropriate to conduct such an inspection prior to clearance, e.g., the manufacturer is not yet ready to commercialize the device. In those circumstances, conducting an inspection soon after clearance may be more appropriate. However, because the circumstances under which conducting a pre-clearance inspection would be appropriate are device-specific, we will implement this recommendation only on a case-by-case basis through device-specific guidance.

- **5.2.2.2 - 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.**

We received comments on this recommendation from industry and consumer and healthcare professional groups. Industry comments on the recommendation expressed concerns about confidential or proprietary information being accessible via a public database. As discussed in Section I above, comments from industry were supportive of the concept of a public database and particularly of including 510(k) summaries, but universally expressed concerns regarding public access to detailed photographs and schematics that contained confidential information because this information could be used by competitors to reverse-engineer products. Industry comments

indicated they would be more comfortable with the database if it did not contain confidential or proprietary information. Comments from some members of industry and consumer and healthcare professional groups were supportive of a database that would help manufacturers select more appropriate predicates and provide access to complete and accurate information.

**POA:** As was stated in the original recommendation, we do not intend to put confidential or proprietary information in this database. We believe part of the confusion that arose regarding this recommendation was due to our use of the term “schematic”, which tends to refer to detailed drawings. Instead, we would request that manufacturers provide a device photograph that is acceptable for public display to be included in the database, primarily to help device manufacturers better identify appropriate predicates for new devices. More detailed photographs or schematics submitted in support of a 510(k) submission would be for internal CDRH reviewer use only and would not be made publicly available as part of a database or under a Freedom of Information Act request. The confidentiality of any photographs provided as part of a 510(k) submission will be preserved. However, given the comments received, we believe it is important to seek additional stakeholder input at a public meeting before we take any steps to implement a scaled-back version of this recommendation to assure that we proceed in a way that addresses the concerns raised and best meets the needs of stakeholders.

#### **IV. Next Steps**

The accompanying chart sets out the following in detail: i) a list of the recommendations we intend to implement or begin to implement in 2011; ii) the projected timeline for completing implementation of certain recommendations in 2011; iii) the achievement of major implementation milestones in 2011 for other recommendations; and iv) our plan to give the IOM an opportunity to provide feedback on selected recommendations should they decide to address these recommendations in their report or through another communication.

For the recommendations that we are implementing, there will be additional opportunities for public input, where appropriate. Recommendations that are regulatory actions — such as draft guidances and proposed regulations — will have their own individual comment periods, which will allow stakeholders to weigh in on the draft proposals before they are finalized. In addition, we will hold a Public Meeting from April 7 - 8, 2011, on our White Oak, Maryland campus to solicit feedback and discuss the implementation of two recommendations: the public posting of device photographs and the development of an online labeling repository.

Throughout the implementation process, we will post regular updates on CDRH’s website. We look forward to working with all of our constituencies as we implement the selected 510(k) and Science recommendations. We believe that these improvements will foster medical device innovation, provide greater regulatory predictability, and enhance patient safety.