CDRH RECOMMENDATION
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. 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.
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."
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.
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.
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).
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.
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. 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).
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 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 necessary to support a substantial equivalence determination.
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.
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.

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.
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.
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.
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.
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 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 crosscutting 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 inhouse 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 Council, described above, which would also oversee the communication of lessons learned to review staff, as well as potential follow-up action.
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.

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.
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.
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.
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.
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.
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 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.
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.
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.
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.

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.
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).
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.
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.