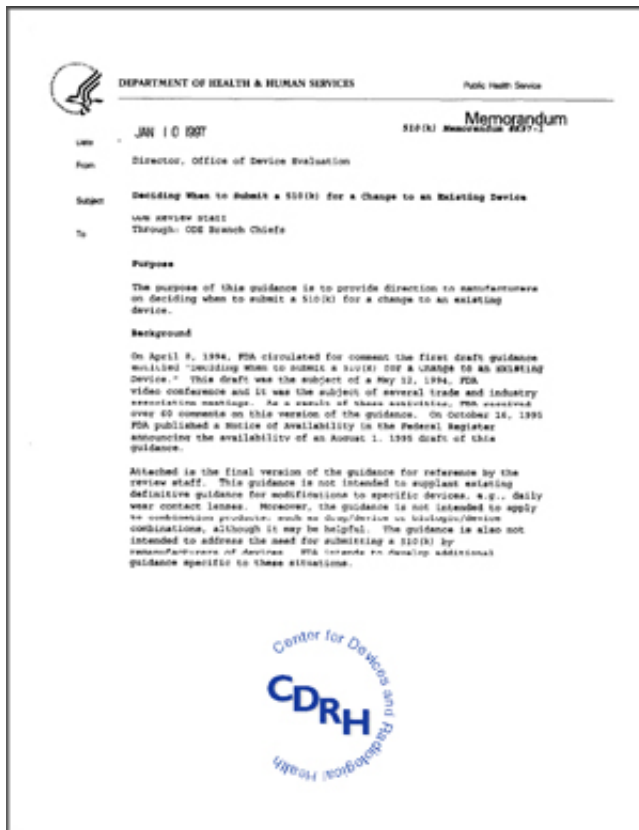


## A guide to FDA's draft guidance on 510(k)s

By *MassDevice*

Created 10/19/2011 - 15:36

October 19, 2011 by *MassDevice*



By *Carolyn Hathaway, Rebecca Brandt, Elizabeth Richards and John Manthei*

On July 27, 2011, the U.S. Food and Drug Administration ("FDA" or "Agency") announced the availability of its long-anticipated draft guidance entitled "510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device," (the "Draft Guidance"). The Draft Guidance, once finalized, will replace the 1997 guidance document, "Deciding When To Submit a 510(k) for a Change to an Existing 510(k)" (the "1997 Guidance"). Like the 1997 Guidance, the Draft Guidance is intended to describe when a new 510(k) premarket notification should be submitted for a change or modification to a legally marketed device.

The issuance of the Draft Guidance comes as part of a comprehensive assessment of the 510(k)

process, which began in September 2009 when FDA convened internal 510(k) working groups to strengthen the 510(k) program and improve consistency in FDA's decision-making process. In August 2010, the Agency working groups published their preliminary reports and recommendations for public comment, and in January 2011 the Center for Devices and Radiological Health ("CDRH") published a "Plan of Action for Implementation of 510(k) and Science Recommendations" (the "Action Plan"). The Action Plan highlighted the need for new guidance on 510(k) modifications, which was expected to be completed by June 15, 2011.

The Agency cited two primary reasons for promulgating the Draft Guidance – (i) to update the 1997 Guidance in light of changing technologies and (ii) to provide greater clarity about changes that do not trigger the need for a new 510(k). Although the FDA has suggested that the new guidance does not change its current policy or practice regarding the submission of 510(k)s for modified devices, it is estimated that, if finalized in its current form, the Draft Guidance will increase the number of modified devices requiring 510(k)s.

**Sign up to get our free newsletters delivered right to your inbox** <sup>[1]</sup>



In addition to eliminating the familiar flow-charts that were a hallmark of the 1997 Guidance, other changes in the Draft Guidance include the following:

- Expansion of the discussion of the devices to which the modified device should be compared.
- Discussion of the Quality Systems Regulations ("QSR") that became effective after the 1997 Guidance was finalized.
- Addition of guidance regarding changes in manufacturing processes that may require a new 510(k).
- Addition of guidance regarding software changes.
- Exclusion of nanotechnology.
- Exclusion of in vitro diagnostic devices.
- Greater Clarity – Less Discretion

FDA issued the Draft Guidance to update and clarify the kinds of changes that will trigger the need for a manufacturer to submit a new 510(k) for a previously cleared device. The Agency asserted that the Draft Guidance does not establish a new policy or practice, but instead, is consistent with FDA's current policy. Some in industry believe, however, that if finalized in its current form, the Draft Guidance is likely to increase the number of 510(k)s submitted for modified devices. Indeed, the examples and recommended analysis presented in the Draft Guidance suggest that more device modifications will likely require a new 510(k) submission. The language in the 1997 Guidance was generally less prescriptive and restrictive when advising that a modification required a new 510(k) submission. In addition, the Draft Guidance eliminates the modification flow charts that many manufacturers relied upon heavily as components of their

own modification analysis procedures. Device manufacturers should review their policies and processes for evaluating device modifications in light of the Draft Guidance.

FDA regulations require a new 510(k) submission when a change or modification to a previously cleared medical device "could significantly affect the safety or effectiveness of the device," or results in a change or modification in the intended use of the device. The 1997 Guidance and the Draft Guidance both provide FDA's thoughts on whether a change could "significantly" affect the safety or the effectiveness of the device. In the Draft Guidance, FDA stresses that the focus of the review is not whether a change does significantly affect the device's safety or effectiveness, but on whether it could have a significant effect. Although the Draft Guidance highlights that whether or not a change does affect a device's safety or effectiveness can be demonstrated by testing, the focus of the modification review should not be the effect of the change. Instead, the Draft Guidance instructs manufacturers to consider whether a change "could" have such an effect. To assist manufacturers in this exercise, the Draft Guidance categorizes the types of changes likely to require a new 510(k). In other words, the Draft Guidance appears to establish a presumption that particular types of changes will require that manufacturers submit a new 510(k) based solely on the nature of the change or modification at issue.

Similar to the 1997 Guidance, the Draft Guidance maintains that a manufacturer may, in the first instance, determine whether or not a new 510(k) is required for modifications made to a previously cleared device, and notes that FDA may review and disagree with the manufacturer's determination. The 1997 Guidance notes explicitly that it is "after all, a guidance document and it is not intended to be prescriptive ... [and was] intended only to provide the logic scheme for enhancing the likelihood of good decisions." Signaling its more prescriptive approach, the Draft Guidance eliminates this language and replaces the goal of minimizing unnecessary 510(k)s that was explicit in the 1997 Guidance with a goal of greater clarity. Consistent with its goal of greater clarity, the Draft Guidance takes a more definitive approach to the circumstances in which it expects that a new 510(k) will be submitted. In doing so, it eliminates much of the discretion that the 1997 Guidance left to the manufacturer. Thus, to the extent a manufacturer assesses a modification and determines that a new 510(k) is not required, it should anticipate having to defend that decision in light of FDA's strong expectation that certain changes will always necessitate a new 510(k).

In describing the modifications for which a 510(k) is required, the Draft Guidance largely eliminates adverbs such as "normally," "usually," and "typically" that were used in the 1997 Guidance. For example, under the 1997 Guidance, "[d]eletion of a contraindication usually requires the submission of a 510(k) prior to effecting the change because this type of labeling change typically expands the indications for use." In the Draft Guidance, FDA eliminates the words "usually" and "typically" to instead clarify that a 510(k) will be required to remove a contraindication from a label: "Manufacturers planning to delete a contraindication should submit a new 510(k) prior to effect the change because this type of labeling change expands the indications for use." Similarly, in device modifications affecting the fundamental scientific technology of the device, the 1997 Guidance provided that "such changes will normally require the submission of a new 510(k)." The Draft Guidance, in contrast, states that "all changes in fundamental scientific technology could significantly affect safety or effectiveness. Therefore such changes require the submission of a new 510(k)." These seemingly minor word changes from the 1997 Guidance eliminate manufacturer discretion for whether or not to submit a 510(k) for these types of changes.

Similarly, the Draft Guidance emphasizes the significance of unintended or "collateral" changes. The 1997 Guidance states that it is to be applied using the "intended changes to the device" and

not to "any unforeseen results of implementing a change." Although the 1997 Guidance notes that such unforeseen results may be a key factor in deciding to submit a 510(k), they are not included in the specification change analysis. In contrast, in discussing changes to device specifications, the Draft Guidance states that "changes to device specifications can significantly affect the performance of a device, and thus significantly affect a device's safety and effectiveness," including those that "may be unintended collateral changes." Thus, under the Draft Guidance, any change in specification will require a new 510(k) even if those changes are unintended.

## Changes Affecting Modification Procedures and Documentation

The Draft Guidance makes a number of additions and changes to "update" the 1997 Guidance. These additions and revisions may also limit a manufacturer's discretion and may significantly alter a manufacturer's longstanding approach to evaluating, documenting, and implementing device modifications. Several of these are discussed below:

**Elimination of Flow Charts:** The Draft Guidance, without explanation, eliminates the flow-charts that were a hallmark of the 1997 Guidance and that have become an integral part of manufacturers' modification analyses and documentation. Indeed, many manufacturers document their modification analyses simply by retaining copies of their decision flow charts. If FDA maintains this approach, companies will need, at a minimum, to revise their procedures for undertaking modification analyses and reconsider the documentation that they maintain to support their decisions.

**QSR Regulations:** When the 1997 Guidance was finalized, the Quality System Regulations at 21 C.F.R. Part 820 had been issued but had not yet become effective. Consequently, the 1997 Guidance does not clearly address the application of the QSR to device modifications other than to note that the then-current good manufacturing practice regulations require documentation, testing, validation, and approval of design changes "that can support the decision on whether to submit a 510(k)." Such validation data and the flow chart analyses frequently constitute a manufacturer's documentation of its modification decisions.

In contrast, the Draft Guidance explicitly ties the documentation and procedural requirements applicable to the modification analysis to the QSR requirements. In addition to noting that the QSR requires documentation and validation or verification of specification changes, the Draft Guidance states that "manufacturers should have a mechanism or standard operating procedure" for evaluating device modifications. Moreover, if the manufacturer determines that it does not need to submit a new 510(k), it should document the basis for its conclusion. The Draft Guidance recommends that manufacturers answer each question posed in the Draft Guidance "to satisfy basic Quality System requirements for documenting device modification" set forth at 21 C.F.R. §§ 820.30 (design changes) and 820.70(b) (production and process changes). Thus, it appears to be FDA's position, that the failure to maintain the "recommended" documentation constitutes a violation of the QSR.

**Comparison to Previously Cleared Device:** Both the 1997 and the Draft Guidance note that, in determining the need to submit a 510(k), the modified device should be compared to the last device to receive 510(k) clearance and that the cumulative effect of all prior modifications that were determined not to require a 510(k) must be considered. The Draft Guidance adds two additional considerations – first, that the modified device should not be compared to multiple devices and, second, that it cannot be compared to any other device produced by the same or another manufacturer. However, in many circumstances, the evolution of a device is not entirely

linear and modifications to a device may lead to multiple new 510(k)s for different current models of the device that have different characteristics. In the past, companies may have compared a modified device that was a hybrid of two or more cleared versions of a device to both of those devices for purposes of determining whether a new 510(k) is required. The Draft Guidance appears to explicitly preclude this approach.

## Updates Reflecting New Technologies

The Draft Guidance includes a number of changes that FDA believes are necessary in light of the changes in medical technologies over the past 15 years. Thus, the Draft Guidance adds or expands references to new technologies such as nanotechnology and software changes and removes discussions of others such as in vitro diagnostics. These changes are discussed briefly below.

**Nanotechnology:** The science and implications of nanotechnology have expanded significantly over the past decade and the use of nanotechnology in medical devices was not even mentioned in the 1997 Guidance Document. In the Draft Guidance, FDA notes that nanotechnology is a new and evolving field for which the Agency has not yet adopted nano-specific criteria to assist medical device manufacturers in evaluating changes to devices incorporating nanotechnology. Indeed, the Draft Guidance notes that, as yet, FDA has not adopted a formal definition of nanotechnology and nanomaterial, instead advising manufacturers to consider (1) whether an engineered substance has at least one dimension in the 1 nm to 100 nm range or (2) whether the substance has properties or effects attributable to its dimensions, even if they fall outside of the nano-range. Thus, in the Draft Guidance, FDA declined to provide criteria for evaluating changes to devices that involve the application of nanotechnology. Instead, FDA expressed its intention to develop additional guidance on this issue and, in the meantime, advised manufacturers to contact the review division on issues relating to nanotechnology.

**Software:** The Draft Guidance notes that changes to device software can have a pervasive effect on the safety and effectiveness of the device and trigger the need for a new 510(k). The 1997 Guidance included software modifications in the general decision tree for technology or performance changes and briefly highlighted software changes in the narrative of the document. The Draft Guidance provides a much greater emphasis on the potential significance of software changes. Specifically, in the discussion of Technology, Engineering, and Performance Changes in the Draft Guidance, FDA adds criteria for consideration when determining whether software changes require a new 510(k), noting that changes to device software that could expand the capability of the device, affect device performance, or could affect a clinical algorithm (defined as software that analyzes, interprets, or uses clinical data) would warrant a new 510(k). The Draft Guidance also notes that Medical Device Data Systems are exempt from 510(k) requirements and are therefore outside the scope of the guidance.

**In Vitro Diagnostic Devices ("IVDs"):** FDA's regulation of IVDs has been evolving since 1997. FDA has issued several draft guidance documents relating to the regulation of IVDs and, at present, this area remains in flux. In this context, the Draft Guidance eliminates the discussion that was included in the 1997 Guidance regarding materials changes for IVDs, presumably requiring the manufacturers to apply the same principles articulated for other medical devices and to contact the Office of In Vitro Diagnostics ("OIVD") with questions.

## Categories of Changes

The 1997 Guidance identifies and addresses four categories of device modifications: Labeling

Changes, Technology Engineering and Performance Changes, Materials Changes, and Materials Changes in IVD Products. The Draft Guidance reorganizes these categories adding a category on Manufacturing Process Changes, eliminating the category for IVD products and shifting, somewhat, the issues addressed in each category. The following sections provide a summary of some of the key differences between the 1997 Guidance and the Draft Guidance.

## Manufacturing Process Changes

The Draft Guidance highlights the regulatory requirement that a new 510(k) be submitted for changes to the manufacturing process that could significantly affect the safety or effectiveness of the device. According to the Draft Guidance, if manufacturing process information was part of the original 510(k) submission and factored into the original clearance decision, "there is a higher likelihood that modified manufacturing process could significantly affect safety or effectiveness and likely require submission of a new 510(k)." This point was not specifically addressed in the 1997 Guidance.

The Draft Guidance does not address the implication of changes to manufacturing processes that were not included in the original 510(k), other than to reiterate its 1997 Guidance regarding changes in packaging, expiration dating, and sterilization. Both provide that changes resulting in a lower sterility assurance level ("SAL") would routinely need a new 510(k) as would those that affect the integrity of device materials. The Draft Guidance affirmatively states that only if the SAL is less than  $10^{-6}$  should a new 510(k) be submitted. The Draft Guidance also requires a new 510(k) for changes to the sterilization method, such as changing from moist heat sterilization to e-beam radiation, as well as for a change that results in a device being provided non-sterile when it was previously sterile, and vice-versa.

## Labeling Changes

Both the Draft Guidance and the 1997 Guidance acknowledge that changes to labeling often pose the most difficult questions for device manufacturers and note that apparently subtle changes can have a significant impact on the safety and effectiveness of the device. The 1997 Guidance concentrates on changes in the indication for use and notes that "other labeling changes are recommended for documentation only." In contrast, the Draft Guidance notes that the term labeling, as defined in the Federal Food, Drug, and Cosmetic Act ("FDCA"), is far broader than just instructions for use and includes "all written, printed or graphic matter on or accompanying the medical device."

Indications for Use: Both the 1997 and the Draft Guidance focus first on whether the change under consideration affects the indications for use. The 1997 Guidance defines "indications for use" as "identify[ing] the target population in a significant portion of which sufficient scientific evidence has demonstrated that the device as labeled will provide clinically significant results and at the same time does not present an unreasonable risk of illness or injury associated with the use of the device." The Draft Guidance focuses instead on how the device is described and defines "indications for use" as "description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient for which the device is intended." In addition, the Draft Guidance does not discuss the distinction between "indications for use" and "intended use," which the 1997 Guidance included. However, both the 1997 Guidance and Draft Guidance highlight FDA concern about changes to the indications for use and agree that changes in this section will most likely require submission of a new 510(k).

The 1997 Guidance provides that a change in the indications for use that limits use within the

currently cleared indication may occur without submission of a new 510(k). The Draft Guidance permits such changes without the submission of a new 510(k) only if the limitation is "due strictly to marketing reasons." If a firm decides to market the device for a more limited indication due to other reasons such as changes made to the device "that affect the removed indication or because of complaints or corrective actions" then, according to the Draft Guidance, the change would be a "major change" requiring a new 510(k).

The Draft Guidance also adds examples of common labeling changes that affect the indications for use and that FDA believes would require submission of a new 510(k). The first of these new examples results in a different outcome than the 1997 Guidance. In the 1997 Guidance, FDA stated that "510(k)s are not necessary to add home use labeling" to a prescription product whose use in the home is accepted medical practice. Under the Draft Guidance, a new 510(k) would be required. Specifically, FDA explains that labeling "changes from prescription use in a clinical setting to prescription use in a home setting" require a 510(k).

In addition, the Draft Guidance would require a 510(k) for changes from general patient populations to specific patient populations (such as a change from an undefined age group to a pediatric population). In the 1997 Guidance, FDA notes that limiting the patient population by age or weight would not require the submission of a new 510(k) where the original indication was for adults and the revised indication is to adults 60 years and older. However, revising the indication from adults to a pediatric population may require the submission of a new 510(k) based on an assessment of whether the change poses any additional risks or expands the use to a new and distinguishable patient population.

**Contraindications for Use:** Both the 1997 Guidance and the Draft Guidance take a similar approach to changes to contraindications. Although FDA recognizes that the addition of a contraindication should be implemented immediately for public health purposes, the new labeling should be submitted to FDA as part of a new 510(k) that is prominently labeled "change being effected." Both guidance documents also recognize that deletion of a contraindication requires the submission of a 510(k) prior to effecting the change because this type of labeling change expands the indications for use.

The Draft Guidance eliminates some of the flexibility reflected in the 1997 Guidance, however. In the 1997 Guidance, FDA stated, "Because we recognize that device labeling often includes contraindications that would more appropriately be warnings or precautions, labeling changes that delete contraindications under such circumstances can be made without the need for a 510(k)." The Draft Guidance no longer permits the removal of contraindications that are more appropriately considered to be warnings or precautions without the submission of a 510(k). As explained below, the Draft Guidance takes the position that the deletion of a warning or precaution warrant a new 510(k) insofar as it could change the intended use and could therefore have a significant effect on safety or effectiveness.

**Instructions for Use:** The 1997 Guidance states that changes to clarify instructions to make the device easier, safer, or more effective to use do not require submission of a new 510(k). The Draft Guidance takes a different approach, which appears to be clearer but which provides less discretion than the earlier guidance. The Draft Guidance states that if the labeling change instructs the user to use the device in a different fashion from that originally cleared, then this could lead to new significant safety risks or less effective use of the device and does constitute a major change in intended use that requires submission of a 510(k).

**Warnings or Precautions:** As noted above, the treatment of changes in warnings and precautions

is an area where the Draft Guidance is somewhat more stringent than the 1997 Guidance. The 1997 Guidance took the position that changes in warnings and precautions would not precipitate the need for a new 510(k), even where the event that precipitated the change was reported under the Medical Device Reporting regulations. The Draft Guidance limits manufacturers' discretion on this point. Under the Draft Guidance, the addition of a warning or precaution would not normally precipitate submission of a new 510(k), but deletion of a warning or precaution could be a change in intended use that affects how a device is used and could therefore have a significant effect on safety and effectiveness. Such deletions would most likely warrant a new 510(k).

**Other Labeling Changes:** The Draft Guidance clarifies that the following labeling changes will not typically require a new 510(k): changes that simply clarify language and do not change the meaning or aesthetic; organizational changes to the way information is displayed; or logo or name changes.

### Changes in Technology / Engineering / Performance Specs

In general, the Draft Guidance re-organizes and re-phrases the specific questions and discussion included within this category in the 1997 Guidance. In many respects, the guidance and criteria in the Draft Guidance are generally consistent with those in the 1997 Guidance. In some instances, however, the language changes in the Draft Guidance limit some of the discretion that manufacturers enjoyed under the 1997 Guidance. In other instances, the Draft Guidance changes the earlier guidance significantly or adds considerations not included in the 1997 Guidance.

For example, the 1997 Guidance states that changes in energy type will "usually" require submission of a new 510(k). In contrast, the Draft Guidance states that changes in energy type "will always have a significant effect on safety and effectiveness because power inputs and outputs are typically critical to proper device function" and that most such changes should be reviewed in a 510(k) prior to marketing. In addition, the Draft Guidance expands "energy type" to include energy output. 1997 Guidance only explicitly contemplated changes to energy input.

In addition, the 1997 Guidance does not explicitly address performance specification changes, other than in the context of changing the method of sterilization. The Draft Guidance advises, however, that changes to performance specifications require a new 510(k) with comparative testing for the modifications, even when the modifications are intended to increase safety or effectiveness or improve performance.

Other modifications addressed in the Draft Guidance include the following:

**Ergonomics or Patient/User Interface:** The Draft Guidance introduces the issue, not explicitly included in the 1997 Guidance, of whether a change in ergonomics or the patient/user interface requires a new 510(k). According to the Draft Guidance, ergonomic changes may or may not require a new 510(k) depending on whether the change can expand how the device will be used or affect how it will perform. Changes intended to increase comfort that do not improve or diminish safety or effectiveness will not warrant a new 510(k). However, if, for example, a surgical handpiece is modified to make the device less bulky and easier to wield by relocating the motor closer to the proximal end of the device, a 510(k) would be warranted because the change in location of the motor "could be too close to the treatment area on the patient or to the user's hand and cause burns, or the mechanical performance of the device could be affected." This example would require the manufacturer to contemplate unintended consequences of the

change and specifically mandates that the unintended consequences be a consideration for whether a new 510(k) is required.

**Dimensional Changes:** The Draft Guidance states that dimensional changes may or may not significantly affect safety or effectiveness, and thus may or may not require a new 510(k). Typically, changes to device dimensions that are related to the performance of the device outside of the cleared dimensional tolerance range have the potential to significantly affect safety or effectiveness. Device dimensions that are modified beyond tolerance ranges will usually warrant a new 510(k).

**Software or Firmware:** The 1997 Guidance references software and firmware changes only in its logic scheme of questions to assist in the determination of whether the change was a routine engineering change, or required a new 510(k). The Draft Guidance addresses these changes more specifically, stating that small changes to device software can have pervasive effects on the safety or effectiveness of a device, triggering the need for a new 510(k) submission, but acknowledges that some low risk changes may be made by following the QSR and documenting the appropriate validation testing. According to the Draft Guidance, the key factors to consider in this determination are whether the software change could expand the capability of the device or affect device performance, or whether the change could affect a clinical algorithm – such changes warrant a new 510(k).

**Receipt, Transmission, or Display of Electrical Signals or Data:** The Draft Guidance states that most changes that impact how the device receives, transmits, or displays electrical signals or data, although seemingly innocuous, have the potential to significantly impact safety or effectiveness by altering data communication quality. Such changes therefore should result in a new 510(k). For example, changing image display from a monitor in clinical setting to portable hand-held device that could be used in any location, would require a new 510(k) as would changing from hard-wired connection of a keyboard to wireless version. The 1997 Guidance does not explicitly discuss this issue.

**Addition of an Aspect of Autonomous or Semi-Autonomous Control:** According to the Draft Guidance, any change that removes control from the user should be reviewed in a new 510(k). The 1997 Guidance does not explicitly discuss this issue.

**Changes to Address a Specific Risk or Failure Mode:** The Draft Guidance states that known or newly identified risks or failure modes, including those to address adverse events or complaints, will usually result in a 510(k). The 1997 Guidance does not explicitly discuss this issue.

**Use in Practice:** In a major change from the 1997 Guidance, the Draft Guidance states that changes that may affect how a device is used in practice may affect the safety or effectiveness of the device. In particular, the Draft Guidance notes that "when the modification could create a reasonable likelihood of off-label use that could cause harm, a new 510(k) should be submitted to allow FDA to determine whether a labeling change is necessary, even if the manufacturer does not intend a change to the indications for use in the labeling." In contrast, the 1997 Guidance assumed the application of its principles to intended changes to the device and not the potentially unforeseen results of implementing a change. If FDA maintains its position that a 510(k) is required to deter potential off-label use where, by definition, such use is not intended, significantly more 510(k) submissions would likely be required.

The Draft Guidance also concludes that modifications that provide new information or data to the user that "could be" used for patient assessment or diagnostic purposes could significantly affect

safety or effectiveness and may necessitate a 510(k) – even if the new patient assessment information is used only as an aid or adjunct to other measures or is considered to be additional information.

In addition, the Draft Guidance clarifies that changes resulting in an alteration to an established medical procedure, use in a new environment (e.g., clinical to home use), and use by a lay person rather than a physician should be reviewed in a new 510(k).

## Materials Changes

In contrast to the 1997 Guidance, the Draft Guidance addresses materials changes by focusing on whether the material contacts the patient in the first instance. If the materials change will not have direct or indirect contact with the patient, no 510(k) will be necessary unless the changes affect the fundamental device technology or performance. The Draft Guidance explains that indirect contact includes materials that have the potential to come into contact with a patient by some intervening material (such as liquid or gas) by first coming into contact with the intervening material, which subsequently comes into contact with the patient. In contrast, the 1997 Guidance focused on whether the device was implanted and, for non-implanted devices, whether it would contact in vivo fluids or tissues. The 1997 Guidance separately addressed material changes for IVDs – this discussion was not included in the Draft Guidance.

The Draft Guidance further clarifies that changes in processing aids, catalysts, and residual contaminants that are not intended to be part of the material but may be introduced by manufacturing, sterilization, and handling may affect material formulation. In contrast, the 1997 Guidance described material formulation changes as changes within a single generic material type that can affect the chemistry, metallurgy, or other property or stability of the material, but did not include changes in processing aids, catalysts, residual contaminants, or manufacturing aids that are not intended to be part of the material.

The Draft Guidance appears to eliminate manufacturers' discretion regarding the submission of a 510(k) for changes to material formulation in patient-contacting devices. According to the Draft Guidance, "a new 510(k) should be submitted for changes in material formulation for patient-contacting devices or device components." The Draft Guidance further notes that most changes to the material formulation of non-patient-contacting materials likely will not warrant a 510(k) – in that case, documentation alone is likely appropriate.

The Draft Guidance also concludes that coating or surface changes or techniques (including chemical formulation, method of application, or surface preparation) significantly affect safety and effectiveness and would require a new 510(k). These include residual contaminants from manufacturing, sterilization, and other processes that can indirectly change the device surface. The 1997 Guidance does not explicitly discuss this issue.

## Clinical Data

The final section of the Draft Guidance states that a "manufacturer's determination that clinical data is needed because bench testing or simulations are not sufficient to assess the safety or effectiveness of a modified device, is a sure sign...that a new 510(k) should be submitted." The 1997 Guidance discussed the need for clinical data in the context of assessing software/firmware changes, and concluded the same thing. The 1997 Guidance further stated that for IVDs, clinical samples may be collected and analyzed to demonstrate that the device continues to conform to performance specifications and a new 510(k) is not required; the Draft Guidance declines to

address the impact on IVDs, stating that IVDs have different testing requirements, and recommends contact with OIVD.

\* \* \* \* \*

Although FDA's 1997 Guidance addressed changes in many of the same areas as the Draft Guidance, the Draft Guidance appears to take a more conservative approach to a few substantive areas that could result in the requirement for submission of more 510(k)s than under the 1997 Guidance. Importantly, the Draft Guidance requires medical device manufacturers to consider the unintended consequences of changes to their device and whether those consequences could "significantly affect safety or effectiveness." Specifically, the Draft Guidance's new discussion of off-label use is sure to have a significant impact if it is retained in the final version of the guidance. Moreover, FDA's efforts to provide greater clarity and transparency appears to have diminished manufacturer discretion regarding whether to submit a new 510(k) for device modifications. As a result, manufacturers should consider how to update and revise policies and procedures for assessing device modifications or changes to ensure that internal policies are consistent with FDA's current thinking on when a new 510(k) is required, as articulated in the Draft Guidance.

The Draft Guidance is intended to supersede the 1997 Guidance once finalized, and FDA is currently accepting comments through October 25, 2011. FDA has stated it will consider all comments submitted by this date before finalizing the guidance. As such, medical device manufacturers that could ultimately be affected by the proposed differences in the Draft Guidance should endeavor to submit comments to aid in shaping the final document. Only time will tell if FDA retains some of the more controversial changes from the 1997 Guidance in the final version of the Draft Guidance.



Carolyn Hathaway is a partner in the Washington, D.C. office of Latham & Watkins. Her practice focuses on matters involving the FDA. In addition to her legal training and practice, Ms. Hathaway has a technical background in chemistry and the biological sciences, and an MBA in health care management. She has extensive experience in technical regulatory matters and has represented pharmaceutical, device, biotechnology, chemical and agrichemical companies at various stages of product development, including preclinical and clinical testing, regulatory approval and commercialization. She has participated in a variety of proceedings before FDA and CMS, and has provided counseling to companies on issues of regulatory compliance and interpretation. Ms. Hathaway also has assisted clients participating in rulemaking proceedings relating to a variety of regulatory issues. She has also worked with trade associations and industry consortia to address specific regulatory issues pertaining to various federal and state laws and initiatives.



Rebecca Brandt is an associate in Latham & Watkins' Houston office. Ms. Brandt focuses her practice on regulatory, transactional and compliance matters involving the medical device, pharmaceutical, biotechnology, food, cosmetic, dietary supplement and healthcare industries. Ms. Brandt has counseled clients on a wide variety of regulatory matters involving the US Food and Drug Administration (FDA), including, among others, pre-market product development; FDA submissions; product promotion and labeling; compliance with good manufacturing practice requirements; and recalls.



Elizabeth Richards is an associate in the Washington, D.C. office of Latham & Watkins where she focuses her practice on regulatory and transactional matters for health care, medical device, pharmaceutical, cosmetic and other biotechnology industry clients. In particular, Ms. Richards has advised on regulatory and compliance issues involved in various stages of the biotechnology product life cycle, including the preclinical, clinical, and post-marketing phases in the US, Europe and Mexico. She has also assisted in compliance counseling for health care entities such as laboratories and health care clinics, and has reviewed agreements regarding preclinical services and clinical trials for pharmaceutical and medical device companies.



John R. Manthei is a partner in the Washington, D.C. office of Latham & Watkins and serves as Global Co-Chair and Washington, D.C. Department Chair of the Healthcare and Life Sciences Practice. His practice focuses on regulatory matters involving the Food and Drug Administration (FDA) for the medical device, pharmaceutical, biotechnology, food and dietary supplement industries.

[Legal News](#) <sup>[2]</sup>, [News Well](#) <sup>[3]</sup>, [510\(k\)](#) <sup>[4]</sup>, [Regulatory/Compliance](#) <sup>[5]</sup>  
[Latham-Watkins](#) <sup>[6]</sup>

[Permalink](#) <sup>[7]</sup>

[Latham-Watkins](#)

© 2010 Massachusetts Medical Devices Journal LLC and its licensors. All rights reserved.  
The material on this site may not be reproduced, distributed, transmitted, cached or otherwise

used, except with the prior written permission of MMDJ.

- [About Us](#)
- [Advertise](#)
- [Contact](#)
- [Directory](#)
- [Privacy Policy](#)
- [User Agreement](#)

---

**Source URL (retrieved on 10/20/2011 - 01:30):** <http://www.massdevice.com/blogs/massdevice/guide-fdas-draft-guidance-510ks>

**Links:**

[1] <http://visitor.r20.constantcontact.com/d.jsp?llr=rhga6adab&p=oi&m=1102763268337>

[2] <http://www.massdevice.com/business-types/legal-news>

[3] <http://www.massdevice.com/business-types/news-well>

[4] <http://www.massdevice.com/business-types/510k>

[5] <http://www.massdevice.com/business-types/regulatorycompliance>

[6] <http://www.massdevice.com/companyorganization/latham-watkins>

[7] <http://www.massdevice.com/blogs/massdevice/guide-fdas-draft-guidance-510ks>