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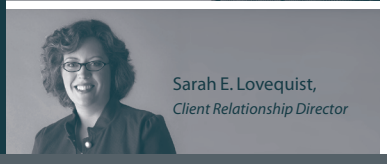

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MIM Reporter

THE REVIEW OF
MEDICAL INFORMATION MANAGEMENT
FOR LITIGATION

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New Year's Regulations from the FDA

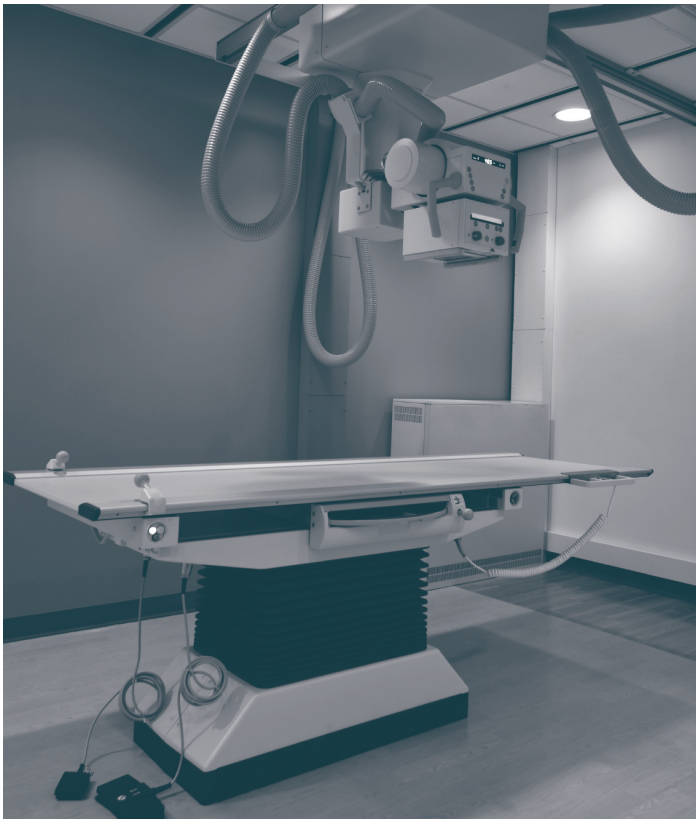
A new year brings new tasks to accomplish and resolutions to keep, and the Food and Drug Administration (FDA) is no exception. While the FDA's "new year" officially began on October 1, 2012[i], medical device manufacturers should know that they are part of the FDA's resolutions. Throughout the coming year device manufacturers should expect continued change and clarification to regulations covering premarket approvals, premarket notification requirements, clinical trials, mobile medical applications, and general medical device classification and review processes.

In July 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act (FDASIA), which included reauthorization of the Medical Device User Fee Amendments of 2012, or MDUFA III. MDUFA III went into effect on October 1, 2012, running through October 1, 2017. As part of MDUFA III, and in return for additional funding, FDA agreed to meet a variety of quantitative and qualitative goals intended to expedite the release to market of safe and effective medical devices. In addition to other responsibilities, FDA agreed to:

- post annually a list of prioritized device guidance documents that the Agency intends to publish within 12 months of the date this list is published each fiscal year (FY)
- post annually a list of device guidance documents that the Agency intends to publish as resources permit each fiscal year
- update FDA's website in a timely manner to reflect the Agency's review of previously published guidance documents, including the deletion of guidance documents that no longer represent the Agency's interpretation of, or policy on, a regulatory issue, and notation of guidance documents that are under review by the Agency
- provide stakeholders an opportunity to provide feedback, including draft language for guidance documents[ii]

MIM Reporter
THE REVIEW OF **MEDICAL INFORMATION MANAGEMENT** FOR LITIGATION

Within the larger FDA is a division of the Office of Medical Products and Tobacco named the Center for Devices and Radiological Health (CDRH). CDRH is responsible for promoting the public health and overseeing and regulating entities that "manufacture, repackage, relabel, and/or import medical devices sold in the United States."[iii] CDRH also regulates medical and non-medical radiation-emitting electronic products. Implementation of the duties set forth in FDASIA and MDUFA III are one of CDRH's top priorities. To ensure that both its individual mission and the purpose of the FDA are fulfilled, CDRH regularly issues strategic priorities to guide its activity each fiscal year.



FY2013 STRATEGIC GOALS

CDRH has prioritized a number of goals for 2013, supported by a strategic plan designed to accomplish each goal. This list includes strengthening CDRH's premarket review process, clarifying its approval and release to market process, enhancing the safety and efficiency of clinical trials, adoption of a connected health care environment that is patient-focused, defining the appropriate regulatory oversight for diagnostic devices that are intrinsically tied to therapeutics, and strengthening all aspects of the regulatory and post-market surveillance process. Most policies are targeted for draft completion by September 30, 2013, with appropriate public comment and implementation periods following thereafter.

By its own admission, people are CDRH's first priority, and the majority of its strategic goals are geared towards improving patient care and public health. That being said, device manufacturers will undoubtedly be impacted by CDRH's goal to solidify its premarket review program, and streamline clinical trials. CDRH aspires to provide "the regulated industry with predictable pathways for the approval of new products," and will do so by finalizing previously issued draft guidance documents by September 30, 2013; 510(k) submissions relating to changes to existing medical devices will be separately addressed.[iv] *Further, by June 30, 2013, a pilot project focusing on ways "to streamline the regulatory pathway from FDA approval to reimbursement" will begin in an effort to reduce time between premarket approval and patient device access.*[v]

Regarding clinical trials and within the same timeframes, CDRH aims to develop policies that will facilitate better and more efficient use of existing premarket registries, and will develop a pilot project that focuses on reducing the time and cost of medical device trials.

What follows is a list of prioritized medical device guidance documents that CDRH anticipates finalizing during Fiscal Year 2013[vi]:

Final Guidance Topics

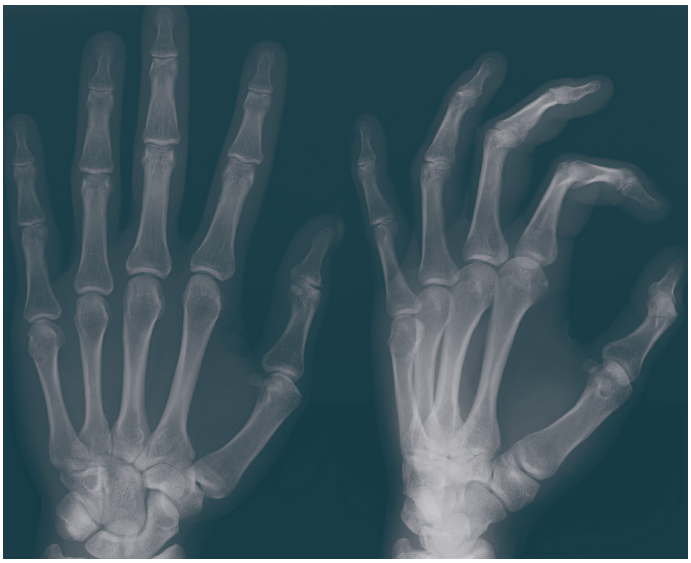
- Refuse to Accept (RTA) Policy for 510(k) Submissions
- Acceptance and Filing Review for Premarket Approval Applications
- Investigational Device Exemptions (IDE) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies
- In Vitro Companion Diagnostic Devices
- Design Considerations for Pivotal Clinical Investigations for Medical Devices
- De Novo Classification Process (Evaluation of Automatic Class III Designation)
- The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications
- CDRH Appeals Processes
- Medical Device Classification Product Codes
- The Pre-Submission Program and Meetings with FDA Staff
- Mobile Medical Applications
- eCopy
- Premarket Notification [510(k)] Submissions for Medical Devices that Include Antimicrobial Agents

Draft Guidance Topics

- Distinguishing and Reporting Medical Device Recalls from Product Enhancements
- Types of Communication During the Review of Medical Device Submissions
- FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations
- eCopy
- Appropriate Use of Voluntary Consensus Standards in Premarket Submissions

CDRH also has a wish list of guidance documents it would like to draft during FY2013, including Benefit-Risk Determinations in Premarket Notifications (510(k)s), Direct to Consumer (DTC) Genetic Testing: IVDs, Transfer of Ownership of a Premarket Notification (510(k)) - Questions and Answers, and Custom Devices, as well as finalizing all existing draft guidance documents. Likewise, guidance documents on topics not listed, but that equally affect public health issues, may alternatively be issued.

While unforeseen circumstances or conditions may prevent CDRH from issuing some or all of the intended guidances, the above list provides device manufacturers with an opportunity to plan operations around anticipated regulations.



CURRENTLY ACTIVE FY2013 FINAL GUIDANCE DOCUMENTS

As a step towards accomplishing its FY2013 strategic goals, CDRH released on December 31, 2012 three final guidance documents; drafts of same were originally circulated for public comment in the Summer and Fall of 2012. As illustrated by the following descriptions, each final guidance covers a more process-oriented aspect of device approval, making each fairly straightforward.

eCopy Program for Medical Device Submissions

FDASIA requires CDRH to issue a guidance document describing the process for submitting an "eCopy" version of a medical device submission,[vii] which is accomplished through CDRH's "eCopy Program for Medical Device Submissions." An eCopy is required for nearly all medical device submissions, including 510(k)s, de novo petitions, PMAs, IDEs, HDEs, pre-submissions, and devices regulated by the Center for Biologics Evaluation and Research (CBER). Although there are limited submissions types exempted from eCopy requirements, the FDA "strongly encourages" companies to submit an eCopy for all exempt submission types.

Of note, an eCopy does not replace hard copy submissions; rather, it is "an exact duplicate of the paper submission, created and submitted on a compact disc (CD), digital video disc (DVD), or a flash drive. An eCopy is accompanied by a paper copy of the signed cover letter and the complete paper submission."[viii] There are exceptions to the "exact duplicate" requirement, such as when "a paper copy is not practical or appropriate for analysis purposes (i.e. raw data and statistical analysis programs, or data line listings to facilitate bioresearch monitoring review) or is not feasible (i.e. videos, x-rays)."[ix] In these limited circumstances, "the eCopy must include all of the required information for FDA review, whereas the paper copy can include a placeholder cross-referencing the location of certain information in the eCopy." In this situation, and to avoid delay in review, the cover letter should describe any differences in the paper and eCopy versions.[x]

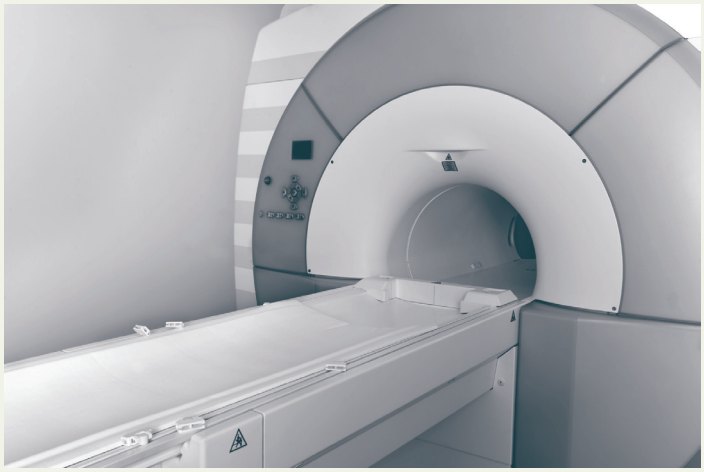
Review of a submission will not begin until FDA receives a valid eCopy, so compliance with FDA's requirements is critical. To this end, FDA has established a free eSubmitter-eCopies tool, available on its website, which FDA "strongly encourage[s]" applicants to use. This tool creates a real-time eCopy that is consistent with the standards set out in the guidance document, and is intended to prevent review delays.

Acceptance and Filing Reviews for Premarket Approval Applications (PMAs)[xi]

Premarket approval (PMA) is the FDA's most stringent level of review and requires a manufacturer to provide valid, scientific evidence (both clinical and non-clinical) that reasonably assures the FDA that the device is safe and effective for its intended use. This guidance document supersedes the criteria previously issued in 2003, with the goal of encouraging quality PMA applications, and allowing FDA staff to concentrate resources on the substantive review of said applications.

This guidance now separates the criteria for PMA filing into acceptance criteria and filing criteria, and provides checklists relative to each set of criteria to help clarify the necessary elements and contents of a complete PMA submission. Submitters should note that acceptance and filing reviews are conducted solely to determine the basic adequacy of the PMA; the submitted information is not evaluated to determine whether there is a "reasonable assurance of safety and effectiveness," but rather is evaluated only based on the checklist criteria.[xii]

To be deemed administratively complete and thus "accepted," the submission should include all organizational and administrative elements contained in the aforementioned checklist, or a rationale for elements determined "not applicable" by the applicant. The acceptance review should be conducted and completed by FDA within 15 calendar days of receipt of the submission, provided that all fees have been paid and a validated eCopy accompanies the submission. Within the 15 day timeframe FDA should provide a written response to the submitter either indicating the submission was accepted or identifying any missing elements; likewise, if the submitter does not hear from FDA within 15 days, the PMA should be considered accepted.[xiii]



Once the submission is deemed administratively complete, FDA staff will undertake a filing review using the criteria in the applicable checklist. Filing reviews should be conducted and completed within 45 calendar days of receipt with written notice to the applicant indicating whether the submission has been filed. Once a submission has been deemed "accepted" and "filed," the application will undergo a substantive review to evaluate "the quality of the content and lead to a decision regarding the safety and effectiveness of the PMA product."[xiv]

Refuse to Accept Policy for 510(k)s

At its most basic, Section 510(k) of the FDCA requires device manufacturers to notify the FDA of their intent to market a medical device at least 90 days in advance of doing so, which allows the FDA to determine whether the device is substantially equivalent to an existing device. This new guidance supersedes CDRH's 1993 Premarket Notification (510(k)) Refuse to Accept (RTA) Policy and its 1994 510(k) Refuse to Accept Procedures blue book memo.

The current guidance adopts a procedure for 510(k)s similar to that described above for PMAs, specifically including an early review based on objective acceptance checklist criteria, and informing the submitter within the first 15 calendar days after receipt of the submission if the submission is administratively complete, or if not, identifying missing elements.[xv]

Assessment of the administrative completeness of the 510(k) occurs during the acceptance review, while assessment of the quality of the submitted information occurs during the substantive review: "during acceptance review, FDA should not consider whether the information provided is sufficient to demonstrate substantial equivalence to a legally marketed predicate device, but only administrative completeness."[xvi]

For FDA to classify the submitted 510(k) as "accepted," all administrative elements identified in the guidance document and appropriate checklist should be included, or the submitter should provide a rationale explaining why certain missing elements are not applicable. As with PMAs, the acceptance review will be conducted and completed within 15 calendar days of FDA receipt of the 510(k) notification. FDA will use the appropriate checklist (traditional, special, or abbreviated) depending on the type of 510(k) submitted, and the submitter will be notified of the outcome in writing. If FDA does not complete the acceptance review within 15 days, "the submitter should be notified in writing that the acceptance review was not completed and the submission is under substantive review." Once acceptance is achieved a substantive review for substantial equivalence may proceed.

During the course of the substantive review, FDA can request any information that may have resulted in an RTA even if FDA provided notice of 510(k) "acceptance." Once the submission is under substantive review the calendar days used to conduct the acceptance review (i.e. up to 15 days) are included within the 60 calendar days to reach the "Substantive Interaction goal" described in the commitment letter for MDUFA III.[xvii]

MANUFACTURER NEXT STEPS

With the impact potentially far reaching, device manufacturers are well-advised to learn and implement the nuances of each guidance document as same is issued, beginning with the released documents mentioned above. For instance,

manufacturers should refer to the "Checklists for Accepting and Filing PMAs" contained in the final guidance document to help ensure their submissions are complete and will be timely accepted and filed. Similarly, submitters should further review the 510(k) checklists to ensure their 510(k)s are complete upon submission.

Finally, a number of drafts relating to the Final Guidance Documents listed above are available for industry review and comment – manufacturers should take advantage of the opportunity to shape the medical device landscape by submitting comments and suggestions to CDRH. If nothing else, CDRH's strategic plan and recently released guidance documents provide manufacturers with a road map of what to expect from the FDA in 2013.

ENDNOTES

i. Federal Fiscal Year 2013 runs from October 1, 2012 through September 30, 2013.

ii. U.S. Department of Health and Human Services, Food and Drug Administration. "CDRH Fiscal Year 2013 (FY2013) Proposed Guidance Development." Center for Devices and Radiological Health. November 23, 2012. January 10, 2013. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/ucm321367.htm.

iii. U.S. Department of Health and Human Services, Food and Drug Administration. "Overview of Device Regulation." August 31, 2009. January 10, 2013. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/default.htm.

iv. U.S. Department of Health and Human Services, Food and Drug Administration. "CDRH 2013 Strategic Priorities." Center for Devices and Radiological Health. December 4, 2012. January 10, 2013. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/ucm330378.htm.

v. Id.

vi. U.S. Department of Health and Human Services, Food and Drug Administration. "CDRH Fiscal Year 2013 (FY2013) Proposed Guidance Development." Center for Devices and Radiological Health. November 23, 2012. January 10, 2013. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/ucm321367.htm.

vii. U.S. Department of Health and Human Services, Food and Drug Administration. "eCopy Program for Medical Device Submissions: Guidance for Industry and Food and Drug Administration Staff." Center for Devices and Radiological Health. December 31, 2012. January 10, 2013. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf.

viii. Id.

ix. Id.

x. Id.

xi. U.S. Department of Health and Human Services, Food and Drug Administration. "Acceptance and Filing Reviews for Premarket Approval Applications (PMAs): Guidance for Industry and Food and Drug Administration Staff." Center for Devices and Radiological Health. December 31, 2012. January 10, 2013. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313368.pdf.

xii. Id.

xiii. Id.

xiv. Id.

xv. U.S. Department of Health and Human Services, Food and Drug Administration. "Refuse to Accept Policy for 510(k)s: Guidance for Industry and Food and Drug Administration Staff." Center for Devices and Radiological Health. December 31, 2012. January 10, 2013. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM315014.pdf.

xvi. Id.

xvii. Id.