Food and Drug Administration

Evaluations and Studies of Premarket Device Reviews under Medical Device User Fee Amendments (MDUFA) II/III for the Food and Drug Administration

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MDUFA II/III Evaluation – Priority Recommendations

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1. INTRODUCTION

The Medical Device User Fee Act of 2012 (MDUFA III) reauthorizes the collection of user fees from industry to support the medical device review process, and to enhance the efficiency of the review process to reduce the total time to bring safe and effective products to market in the United States. Pursuant to the Performance Goals and Procedures adopted under MDUFA III, the Food and Drug Administration (FDA) agreed to participate with the medical device industry in a comprehensive independent assessment of the process for the review of medical device submissions. The assessment was specified to be performed in two phases, and to consist of a technical analysis, a management assessment, and program evaluation. The first phase, which takes place over a one-year period, involves an assessment of the medical device submission review processes implemented by FDA as a result of the MDUFA III negotiations, including Refuse to Accept (RTA), Substantive Interaction (SI), Interactive Review (IR) and Missed MDUFA Decision (MMD) communication.[1] In addition, the first phase includes an assessment of IT infrastructure, training and retention policies and practices, and FDA management systems, while the second phase will entail an evaluation of FDA's implementation of selected recommendations resulting from the assessments performed in the first phase. The MDUFA III Commitment Letter specifies that the independent assessment will provide findings on a set of priority recommendations (i.e., those likely to have a significant impact on review times) within six months of contract award, and final recommendations for the full evaluation within one year. The priority recommendations address key areas of concern identified by industry and FDA, and are intended to resolve issues that would otherwise impede the success of the MDUFA III review processes going forward.

The priority recommendations and suggested actions in this document, derived from work conducted to date, examine issues that have not yet been fully addressed by the new MDUFA III processes and represent potential opportunities for improvement as resources permit. Additional evaluations will continue through the remainder of the first phase of the study, and will culminate with the Final Report and Recommendations, which will be made public in the latter half of 2014.

2. METHODOLOGY

According to the MDUFA III Commitment Letter, the key objective of this task was to develop a set of recommendations for FDA to implement with the potential to have a significant impact on review times. To achieve this objective, this assessment consisted of the following activities:

- Identify issues from the MDUFA II timeframe contributing to unintended outcomes (e.g., longer than average Total Time to Decision (TTD), multiple review cycles, missed goal dates)
- Evaluate the design of major new MDUFA III processes for their potential to address the identified issues and for consistency with quality management (QM) principles
- Characterize and evaluate the MDUFA III enhancements to IT systems and training programs

Booz Allen identified and analyzed review process issues from the MDUFA II timeframe in order to assess whether they were addressed with the implementation of new MDUFA III processes or systems. These issues were identified from a variety of primary and secondary sources including: 1) a literature review comprised of industry reports, MDUFA III negotiation meeting minutes, and published FDA studies, among others; 2) focus groups with FDA and industry stakeholders; 3) interviews with Center for Devices and Radiological Health (CDRH) staff; 4) an in-depth review of 510(k) and Premarket Approval (PMA) submissions that had a longer than average TTD received and reviewed in FY2011-12; and 5) a Lead Reviewer survey. The relative significance of each unaddressed issue was assessed according to perceived importance to industry, impact on review times and estimated level of FDA resources required to address the issue. The highest ranking issues were considered for priority recommendations to be addressed by FDA.

We conducted interviews with FDA staff to evaluate the design of the review processes with respect to high-level industry-recognized quality management principles that were found in ISO 9001:2008, FDA Staff Manual Guide (SMG) 2020, and the newly-created CDRH Quality Management Framework. This quality assessment was not

[1] Our preliminary analysis has shown a decrease in review times since implementation of MDUFA III, and further analysis will be performed to more fully assess the impact and potential unintended consequences of these processes.

intended to be an audit, and thus for our assessment we adapted and qualitatively evaluated only the components we determined to be meaningful to CDRH premarket submission review processes. The CDRH IT systems and reviewer training programs were characterized and assessed for gaps in efficiency and best practices. We evaluated three CDRH IT systems that support MDUFA III: CDRH Center Tracking System (CTS), Image2000+, and DocMan.[2] In addition to hands-on use of these systems, we evaluated a previously-conducted CDRH survey, Quick Guides, Cheat Sheets, and Reference Guides provided to staff for support of the integration of tools into the MDUFA III review process. Additionally, we interviewed CDRH staff and conducted a Lead Reviewer survey to gain insight into user experience and ascertain challenges with integration.

Booz Allen also characterized the four CDRH training programs that were most pertinent: Reviewer Certification Program (RCP), Leadership Enhancement and Development Program (LEAD), Experiential Learning Program (ELP), and Specialized Training Program (or *ad hoc*). We applied the industry gold standard for training evaluation (Kirkpatrick's Four Levels), as well as industry best practices, to assess each of these programs. Training modules provided during MDUFA III implementation, and later incorporated into RCP, were also evaluated to determine whether key process elements were built into the training. Potential recommendations identified from each of these analyses were evaluated against concerns voiced by industry and FDA stakeholders, and those with the most significant impact were included in the priority recommendations.

3. KEY FINDINGS AND PRIORITY RECOMMENDATIONS

Based on our preliminary assessment, we have identified the following priority recommendations for FDA to improve the efficiency and review times of the medical device submission review process:

- Develop criteria and establish mechanisms to improve consistency in decision making throughout the review process
- Provide mandatory full staff training for the three primary IT systems that support MDUFA III reviews
- Identify metrics and incorporate methods to better assess review process training satisfaction, learning, and staff behavior changes
- Adopt a holistic, multi-pronged approach to address five quality component areas to standardize process lifecycle management activities and improve consistency of reviews

The following sections provide additional detail and rationale for each of the priority recommendations. We have also provided suggestions for specific actions that FDA might take to address each recommendation, as resources are available, however FDA may determine at their discretion to take action on these recommendations in alternative ways.

3.1 Develop criteria and establish mechanisms to improve consistency in decision-making throughout the review process

A recurring issue that was identified during our analyses was inconsistent decision-making throughout various stages of the review process, in particular a lack of transparency in thresholds or requirements used to trigger additional information (AI) requests. In addition, industry stakeholders reported inconsistencies between reviewers referencing outdated guidance during submission reviews, as well as reviewers referencing new standards that were not yet released at the time of original submission. Development of tools, criteria and/or mechanisms for assessing and ensuring the consistency of review processes would help ameliorate this issue. For example, Lead Reviewers could reference any applicable guidance or standards prior to or during the time of the AI request to help applicants better understand the scientific and regulatory basis for AI requests when they occur. More broadly, Lead Reviewers might explain which guidances and standards they intend to use for a given submission review, and clearly indicate whether applicants would be subject to any new standards or guidance updates that are released during a submission review. Development of a standard AI request checklist could clarify to applicants the categories of deficiencies that applicants may be subject to receiving. Regularly-occurring working

[2] DocMan is a repository that enables collaborative review by review staff and contains communications between FDA and applicants; Image2000+ serves as the repository for all official and finalized documents at CDRH; CTS serves as CDRH's central document tracking tool for premarket submissions.

groups of Lead Reviewers and Master Reviewers within review branches could be convened to develop a standard working list of criteria for decision making (e.g., within a review branch) that may evolve as technological advancements occur.

3.2 Provide mandatory training for the three primary IT systems that support MDUFA III reviews

New IT infrastructure systems, as well as system upgrades, were developed in support of MDUFA III process changes for streamlining reviews and providing tools for new procedures. While reviewers were offered training prior to October 1, 2012, awareness and retention of knowledge regarding changes to specific review processes varied, based on focus groups and interviews with CDRH staff. For example, users reported uncertainty about which documents to store in DocMan, where to store them, and which work processes would be integrated with DocMan capabilities. While CTS modules were also introduced to aid in managing goal dates and identifying where submissions were in the review process, some users reported that the new, multiple date fields were confusing. From the perspective of Lead Reviewers, IT training had a significant positive effect on facilitating more efficient reviews. Of those surveyed, 53% who reported having received training on CTS, Image2000+, and DocMan indicated that it eased review, while 7% said it detracted from review. By contrast, among those who reported that they did not receive the IT training, only 12% said it eased the review, while 41% said it detracted from the review process. Although only a limited sample of responses, this sharp contrast suggests that training has a significant impact on the effectiveness of the new systems implemented, and we recommend that CDRH ensure all reviewers complete the appropriate system training courses.

3.3 Identify metrics and incorporate methods to better assess review process training satisfaction, learning, and staff behavior changes

As a result of MDUFA III requirements to increase knowledge on submission review for both new and experienced staff, FDA launched a series of new training programs. Our analysis of the four training programs uncovered gaps in FDA's ability to objectively assess the impact of learning and the extent to which participants' review behaviors changed as a result of training. This is an integral component of successful training program evaluation, and a recognized industry best practice. Training administrators need to understand whether training courses are meeting set objectives, and if not, what aspects need to be modified to accomplish that goal. We conducted and analyzed a preliminary survey of Lead Reviewers, in which 63% indicated it helped with the RTA process, and 77% indicated it helped with SI/IR processes. More timely, comprehensive, and detailed surveys could provide FDA with information to tailor and refine their training programs to be more effective. In addition, post-training surveys and/or interviews regarding participants' experience with integrating the knowledge learned can serve as a valuable resource in validating training or identifying a need for change. Therefore, we recommend that the FDA identify metrics and incorporate methods to better assess review process training satisfaction, learning, and staff behavior changes.

3.4 Adopt a holistic, multi-pronged approach to address five quality component areas to standardize process lifecycle management activities and improve consistency of reviews

The MDUFA III commitment letter emphasized an evaluation of FDA's premarket review processes using a quality framework drawing from accepted quality system standards. The current CDRH QM Framework is in a nascent stage, and was therefore not mature enough to use as an evaluation standard. We instead referenced standard quality components (i.e., Senior Management Responsibility, Resource Management, Document Control, Process Improvement, and System Evaluation) and adapted them to include only elements most meaningful to assessing the design of various FDA processes. From our evaluation of QM processes, we derived the following specific recommendations:

- **Senior Management: Document and communicate a mechanism for issue accountability and follow-up**

  The MDUFA III Implementation Steering Committee was formed as a result of MDUFA III, and was tasked with coordinating efforts from various levels of management to determine how each new process would be operationalized in CDRH. Senior management monitors the implementation of the processes and reviews new issues as they arise through existing mechanisms. Each level of management is accountable to ensure successful process implementation and to raise and resolve issues. However, this feedback loop is not formally documented (e.g., the process to intervene on submission issues), which can result in missed opportunities and ambiguity among different management levels to assume all of the necessary steps to see through all issues to resolution. We recommend that CDRH formally document the issue resolution pathway and communicate this process to the review staff, to promote accountability and facilitate follow-up on raised issues. In addition, we recommend that FDA identify points of contact who are able to dedicate time for providing oversight of implementation of an integrated set of quality steps to ensure FDA progresses in each component area.

- **Resource Management: Deploy formal, regularly-scheduled training on new review processes to standardize awareness. Use quantitative methods to assess understanding and activation of behavioral changes**

  The training recommendations detailed in section 3.3 would address this particular QM issue. We deemed it to be sufficiently significant to elevate it to a priority recommendation.

- **Document Management: Deploy planned document control system enhancements (e.g., CTS, DocMan, Image2000+, SharePoint) using a quality-oriented focus to optimize the utility of system changes to all review staff**

  We investigated the various document control IT systems (i.e., CTS, DocMan, Image2000+) for quality in process design. We found that CDRH employs various mechanisms for introducing quality into its document control and document management processes (e.g., there are methods to store submission review templates, reference guides, and collaborative review materials; access controls are in place; there are mechanisms to notify staff of document updates). However, interviews with senior management confirm that inconsistencies within document control elements detract from review performance. For example, DocMan folders often contain many duplicative and/or outdated documents (e.g., three versions of the same summary but with different reviewer/Branch Chief/Division Director signatures). This is not the intended practice and results in errors and inefficiencies when performing document searches. To address this issue, we refer to the priority recommendation in Section 3.2 to provide mandatory full staff training on the appropriate use of document control IT systems to facilitate consistent use and enable efficient reviews. Once complete, an audit of DocMan usage of selected submissions would identify any improvements in consistency of use among review staff. eRooms represent another document control system currently used by staff to reference program and division-specific templates, Standard Operating Procedures (SOPs), checklists, process flows, and user guides in support of submission review processes, but content in eRooms is anticipated to be migrated to SharePoint in the near-term. When this and other important document control system transitions and/or upgrades are made that impact review processes, we recommend that CDRH focus on incorporating quality management components into its roll-out strategy to ensure that these upgrades are positioned for successful use (e.g., migration and roll-out should include required senior management oversight, staff training/workshops to ensure staff may adequately leverage new system functionality, clear mechanisms for staff to raise issues encountered from system use, methods for staff to pilot the system and provide continuous feedback, mechanisms in place to make improvements, and ways in which to assess utility of the system).

- **Corrective and Preventive Action (CAPA) and Continuous Process Improvement (CPI): Develop a more formal method for logging, prioritizing, tracking, communicating and providing feedback on non-CAPA issues and improvement ideas**

  Our review found that the Office of Device Evaluation (ODE) has implemented a CAPA database to resolve issues that impact multiple Divisions. However, for non-CAPA (i.e., Division-specific) issues, there is currently no formal method to log, track, or prioritize issues, or communicate feedback. For example,

staff currently may raise and address non-CAPA issues but do not use a database or employ other systematic methods to manage and record issue resolution. Standard methods across divisions do not exist to log, review, and close out suggestions for process improvement. We recommend that CDRH develop a formal method to be applied consistently across divisions for tracking issues that do not rise to the level of a CAPA, in order to ensure that they are properly attended to and resolved.

- **System Evaluation: Identify and develop internal metrics to monitor the quality and effectiveness of review processes and facilitate continuous process improvement**

  CDRH senior management diligently monitors and reports on submission status, and relies heavily on MDUFA goal milestones for evaluating progress and success. For example, senior management regularly tracks performance trends to identify changes in TTD over time, and also uses MDUFA goal milestone data to identify any submission issues that must be addressed with Branch Chiefs and Division Directors. CDRH also performs periodic *ad hoc* audits on certain processes (e.g., RTA audit). Program operations staff (POS) have noticed that for several submissions that did not meet their MDUFA goal dates, milestones were missed earlier in the process. As a result, program operations staff now pay more attention to these indicators and send reminders to Lead Reviewers of upcoming due dates based on workload reports from the CDRH *Ad Hoc* Reporting System (CARS) and CTS. While this mechanism may work to identify some submissions at risk for longer review times, more granular internal metrics are needed to ensure the quality and effectiveness of sub-processes (e.g., RTA or IR) within the larger submission review process. To this end, we recommend that CDRH identify internal metrics to support the monitoring process and facilitate continuous process improvement.