FDA – Industry MDUFA IV Reauthorization Meeting
October 1, 2015, 9:45 am – 4:00 pm
FDA White Oak Building 66, Silver Spring, MD
Room 4404

Purpose
To discuss MDUFA IV reauthorization.

Participants

FDA

Malcolm Bertoni	Office of the Commissioner (OC)
Marc Caden	Office of Chief Counsel (OCC)
Joni Foy	Center for Devices and Radiological Health (CDRH)
Sonja Fulmer	CDRH
Elizabeth Hillebrenner	CDRH
Louise Howe	OCC
Aaron Josephson	CDRH
Sheryl Kochman	Center for Biologics Evaluation and Research (CBER)
Toby Lowe	CDRH
Thinh Nguyen	Office of Combination Products (OCP)
Geeta Pamidimukkala	CDRH
Ramesh Menon	Office of Legislation (OL)
Don St. Pierre	CDRH
Darian Tarver	OC
Kim Worthington	CDRH
Jacquline Yancy	CDRH
Barb Zimmerman	CDRH

FDA Subject Matter Experts (specialists participating on particular topics)

Sara Aguel	CDRH
Felipe Aguel	CDRH
Nancy Braier	CDRH
Linda Godfrey	CDRH
Charles Haggart	CDRH
Jerry Logue	CDRH
Brendan O'Leary	CDRH
Eric Rechen	CDRH

Industry

Hans Beinke	Siemens (representing MITA)
Nathan Brown	Akin Gump (representing AdvaMed)
Phil Desjardins	Johnson & Johnson (representing AdvaMed)
Allison Giles	Cook (representing MDMA)
Megan Hayes	Medical Imaging Technology Alliance (MITA)
Donald Horton	Laboratory Corporation of America Holdings (representing ACLA)
Tamima Itani	Boston Scientific (representing MDMA)
Mark Leahey	Medical Device Manufacturers Association (MDMA)
Michael Pfleger	Alcon (representing AdvaMed)
Jim Ruger	Quest Diagnostics (representing ACLA)
Paul Sheives	American Clinical Laboratories Association (ACLA)
Patricia Shrader	Medtronic (representing AdvaMed)
Janet Trunzo	Advanced Medical Technology Association (AdvaMed)
Diane Wurzburger	GE Healthcare (representing MITA)

Meeting Start Time: 9:45 am

Executive Summary

At the second user fee negotiation meeting, FDA and Industry discussed FDA's response to Industry's data request, reviewed CDRH information systems for premarket reviews, discussed the implementation of the Independent Assessment, and discussed additional financial analysis. These discussions provided additional contextual information to support upcoming consideration of proposals.

Discussion of FDA's Response to Industry's Data Request

FDA presented key findings from FDA's response to Industry's data request. FDA described the results of an analysis of pre-submissions for IDEs, based on an audit sample of two cohorts representing two different time periods (fiscal year 2013 and part of fiscal year 2014). FDA determined that IDEs with pre-submissions have a greater likelihood of first cycle approval. Although the available data support the conclusion that IDEs with pre-submissions have a greater likelihood of approval, the significance of this conclusion is complicated by the fact that data show it can take longer for an IDE study to be approved when it was preceded by a pre-submission. FDA noted this is likely because pre-submissions are associated with more challenging IDE studies, whereas less challenging IDE studies often do not involve pre-submissions. This indicates that the set of IDEs associated with pre-submissions may have different characteristics than those without, which may inflate their time to approval. FDA and Industry agree that more analysis would be needed to test this hypothesis, and that the inability of FDA's IT systems to efficiently generate clean data hinders a careful analysis.

Another key finding was that Q-submission and *de novo* workload has been increasing. Industry noted that more data should be reviewed to determine if the total number of pre-submissions is starting to level out.

FDA described the trend of increasing numbers of pre-submissions and submission issue meetings (SIMs). Despite increasing numbers of submissions for which there is no fee, FDA has maintained performance goals for these submission types. FDA noted another trend of reviewers providing feedback prior to pre-submission meetings (as contemplated in the MDUFAIII commitment letter) more frequently in FY 2015 than prior years. FDA further noted that Industry has expressed appreciation and value in receiving from FDA this early feedback. Industry was interested in the likelihood of approval and approval times for all submission types with pre-submissions. FDA explained that it can be difficult to get that information because the linking of pre-submissions to submissions is incomplete and sometimes confounded due to limitations of FDA's IT systems.

In response to Industry's request at the September 9 meeting for additional information on the number of guidance documents published by CDRH, FDA presented a summary on the guidance documents that have been issued during MDUFAIII. The summary included the numbers of guidance documents that were revisions to existing guidance documents, guidance on special controls, guidance documents mandated by legislation, or other CDRH initiatives. In response to a question, FDA explained that draft and final guidances are counted separately. Industry appreciated FDA's effort to provide greater clarity via revisions of existing guidance documents. However, industry did note that the significant number of new guidances can inject more uncertainty since many are associated with new initiatives that require FDA staff and industry time to address. During this discussion ACLA expressed concerns about the use of guidance in lieu of formal comment and rulemaking for substantial policy changes. In response, FDA noted that policy statements are exempt from the Administrative Procedures Act notice and comment rulemaking procedures, whether or not there is a change in policy and whether or not that change is significant. Further, in accordance with its Good Guidance Practices, FDA regularly communicates its policies, including significant changes in policies, through guidance documents. MITA requested that the FDA consider additional follow-up from the Guidance Workshop that was held in 2014.[1] In addition, industry noted that guidance documents and standards recognition has an impact on product development and requested that FDA consider implementation timelines for new guidances and recognized standards, where appropriate.

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[1] CDRH Fiscal Year 2015 (FY 2015) Proposed Guidance Development and Focused Retrospective Review of Final Guidance available at
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/ucm321367.htm

CDRH Systems for Premarket Reviews

FDA presented an overview of the CDRH premarket IT systems to further explain in the data that are available and the capabilities and limitations of the CDRH systems that support premarket reviews. FDA noted the premarket systems are designed to focus on tracking information that is needed to manage to and report on MDUFA performance commitments. The systems are complex because the various premarket submission review pathways require taking into account different technical issues and regulatory requirements, which drive different business rules and operational procedures. Moreover, the systems are designed to manage data from the three different MDUFA reauthorization periods as well as the pre-MDUFA era. There are complexities due to transitions from legacy technologies to newer technologies, numerous interdependent systems, a need to support backward compatibility when implementing new programs, and a recent transition from paper to electronic reviews and decision letters. All this complexity means that changing or adding data fields must be done very carefully, with consideration of the costs, benefits, impact on review management, and other tradeoffs.

During this presentation, FDA noted where systems require manual data entry, which data fields are validated, and how information is transferred between systems. Industry asked questions about how sponsor information is entered into the systems and if submissions are linked to Q-submissions. FDA explained that sponsor information, including whether or not there is a related submission, is submitted on a voluntary form (Form 3514). The identification of related submissions is not automatically validated or used to formally link submissions, but is instead used as a flexible tool to aid managers in assigning submissions to reviewers who already may have familiarity with that type of device, and to assist reviewers in performing consistent reviews.

Implementation of Independent Assessment

FDA presented a summary of CDRH's implementation of the Center's Plan of Action to address the recommendations in Booz Allen Hamilton's MDUFA II/III Evaluation. FDA summarized the eleven recommendations for FDA to improve the efficiency and review times of the medical device submission review process. The five categories of recommendations are Quality Management, Evaluation of Review Process, Evaluation of IT Infrastructure and Workload Tools, Evaluation of Training Programs, and Assessment of Staff Turnover. CDRH has committed to address specific BAH recommendations under Stage 1 of the Plan of Action. To further enhance the efficiency of the review process, CDRH outlined additional long-term actions under Stage 2 of the Plan of Action that the Center plans to address as resources permit. All actions are consistent with the CDRH Quality Management Framework and were conducted with a quality systems approach, including evaluating customer requirements, performing gap analyses, developing and prioritizing solutions, implementing the action, verifying effectiveness, and assuring continuous improvement.

FDA shared progress on each of the recommendations and discussed the procedures and improvements CDRH has implemented. CDRH has completed Stage 1 for seven of the eleven recommendations, including all four projects under the Quality Management recommendation. FDA projects that all Stage 1 actions will be met by December 2015. Resources permitting, CDRH will continue to implement Stage 2 actions.

In response to the Corrective and Preventive Action (CAPA) and Continuous Process Improvement (CPI) Quality Management recommendation, FDA implemented the FEEDBACK✓CDRH program. FDA described how this program incorporates feedback from staff, prioritizes the feedback, and ensures process improvements to improve the quality of products and services. FDA discussed how the program addresses CAPA and non-CAPA issues and how the resolution of these issues is transparent to all staff. Furthermore, FDA described how feedback collected from the external Customer Service Survey is incorporated into the FEEDBACK✓CDRH program. In addition to this program, FDA has developed many Standard Operating Procedures (SOPs) and Work Instructions to address the CAPA/CPI recommendation; these actions complete Stages 1 and 2 of the Plan of Action to address this recommendation.

In the Evaluation of Review Process category of recommendations, CDRH has completed Stage 1 of the Refuse To Accept (RTA) recommendation to improve awareness of and clarity around Administrative requirements for 510(k) submissions, the withdrawal recommendation to analyze and mitigate causes of withdrawn submissions, and the communication recommendation to implement a consistent practice for communicating early and frequently with sponsors.

In the IT and Workload Management category of recommendations, CDRH has completed Stage 1 of the IT training recommendation to ensure all reviewers complete training for the three primary IT systems and the workload management recommendation to provide support tools for managers to understand reviewer workload. The recommendation to provide increased clarity on the eCopy program to improve submission structure is in progress.

The actions to implement the Training Program recommendations consistent with the Kirkpatrick maturity model are in progress. FDA described the procedures that have been developed to assess Kirkpatrick Levels 1 and 2 and discussed additional procedures that are under development for Kirkpatrick Levels 3 and 4 and on Informal Training Procedures.

FDA discussed the procedures that are under development to address the Staff Turnover recommendation, including succession planning and transition planning. Industry and FDA discussed the challenges associated with staff turnover and agreed that it is important not only to understand the reasons for turnover, but also to be able to address the impact of staff and manager turnover. FDA asked Industry to share information on their staff turnover rates.

In order to address the recommendation to develop criteria and establish mechanisms to improve consistency in decision-making throughout the review process, CDRH is developing a systems approach to establish a quality-based infrastructure to improve management of the review

process. FDA described the systems approach, which incorporates many elements of other recommendations, to ensure consistency and predictability throughout the review process. CDRH has completed Stage 1 of this recommendation through the establishment of a Charter for the Quality Management Board, which includes subcommittees on Quality Management and CPI, Review Tools and Templates, Focal Point Program, and Premarket Review Policies and Practices. The actions to complete this recommendation also include the development and phased implementation of a guided 510(k) review tool, the SMART template, to further ensure consistency and predictability in the review process. In addition, CDRH has established Management Oversight Procedures to provide process controls at Critical Control Points, including Acceptance review, Pre-substantive interaction, Major Deficiency/Additional Information, Consult Requests, Advisory Panel, and Final Decision.

Industry expressed interest in the SMART template for the guided review and the Critical Control Points addressed through the Management Oversight Procedure. FDA agreed to share the SMART template with Industry. FDA responded to questions on what questions and triggers are included in the procedure and template. Industry and FDA agree that independent and qualified audits are a critical part of Quality Management and are necessary to ensure that processes are followed for consistent reviews.

Financial Analysis

FDA presented additional financial analysis, including a description of the medical device program resource environment, carryover balances, and one-time costs and efficiencies. FDA noted that there was a decrease in the Budget Authority (BA) appropriations for medical devices in FY 2013 due to sequestration, and FDA has met the appropriation trigger related to the Devices and Radiological Health line of the budget each year of MDUFA III thus far. FDA described the components of the FY 2014 funding sources for the total device program. FDA noted that BA appropriations in FY 2016 and FY 2017 are highly uncertain and the amount of BA has been flat over the past five years.

FDA presented a summary of FY 2014 MDUFA carryover balance. FDA and Industry discussed the reasons for collections that were not appropriated during FY 2008 to FY 2012.

FDA presented an expanded explanation of the estimated amount of user fees needed throughout MDUFA IV to maintain the level of staffing and other activities supported by MDUFA III user fees in FY 2017 (the final year of MDUFA III), under current payroll and inflation assumptions. FDA presented this estimate at the first negotiation meeting, and Industry requested further discussion on this topic. FDA presented an explanation of how the current MDUFA III fees were constructed, which forms the basis for the FY 2017 baseline going into MDUFA IV. Under the currently authorized MDUFA III agreement, FDA is authorized to collect $596 million in fees, plus inflation adjustments, spanning the five years of FY 2013 through FY 2017. Of that $596 million, $368 million supports the base from the previous MDUFA II agreement. In order

to achieve the performance goals in MDUFA III, the current agreement provides an additional $211 million for 208 full time employees (FTE). Additionally, MDUFA III provides $16.5 million for targeted supporting costs.

FDA further described what comprises the $16.5 million in targeted supporting costs: training costs for the implementation of MDUFA III programs; costs for IT enhancements; and the cost of the Independent Assessment. The training costs include training for implementing MDUFA III review processes and timeframes, reviewer certification program, experiential learning program, customer service training, implementation of Kirkpatrick levels one and two training programs, and expanded Leadership Enhancement and Development (LEAD) program. FDA considers many aspects of training and IT enhancements as on-going costs, and noted that the total device review program IT costs were predominantly supported by BA. IT enhancements and Independent Assessment costs were spread over the first four years of MDUFA III and were not part of the FY 2017 baseline, hence they were not part of the MDUFA IV baseline projection. Industry raised the point that implementing many of the process improvements under MDUFA III and the additional enhancements as a result of the independent assessment should result in efficiencies. FDA noted that a discussion of efficiencies that may be realized from process improvements under MDUFA III will require a deeper discussion of workload and performance levels, which FDA will attempt to address as part of its proposal analysis.

Discussion

FDA and Industry reiterated agreement that the medical device program has improved and is heading in a positive direction. At the conclusion of the meeting, FDA and Industry agreed to determine the schedule for negotiation meetings in 2016. FDA agreed to provide additional information on the 510(k) and *de novo* program as requested by Industry prior to the next meeting. FDA and Industry discussed the agenda for the next negotiation meeting in November. The parties discussed when they expect to be ready to present their respective proposals. [After the meeting, the parties confirmed that they will be ready to present their respective proposals on November 18.]

Next Meeting

The next meeting is scheduled on November 18, 2015.

Meeting End Time: 4:00 pm