FDA – Industry MDUFA IV Reauthorization Meeting
January 20, 2016; 9:30 am – 3:45 pm
FDA White Oak Building 66, Silver Spring, MD
Room 4404

Purpose

To discuss details of FDA's and Industry's proposal packages for 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)
Thinh Nguyen	Office of Combination Products (OCP)
Geeta Pamidimukkala	CDRH
Prakash Rath	Office of Legislation (OL)
Don St. Pierre	CDRH
Darian Tarver	OC
Peter Tobin	CDRH
Kim Worthington	CDRH
Jacquline Yancy	CDRH
Barb Zimmerman	CDRH

Industry

Hans Beinke	Siemens (representing MITA)
Nathan Brown	Akin Gump (representing AdvaMed)
Phil Desjardins	Johnson & Johnson (representing AdvaMed)
Sergio Gadaleta	Becton, Dickinson (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)
Paul Sheives	American Clinical Laboratory Association (ACLA)

Patricia Shrader	Medtronic (representing AdvaMed)
Janet Trunzo	Advanced Medical Technology Association (AdvaMed)
Diane Wurzburger	GE Healthcare (representing MITA)

Meeting Start Time: 9:30 am

Executive Summary

During the January 20, 2016 user fee negotiation meeting, FDA and Industry discussed the details of FDA's cost estimate of Industry's proposals, as understood by FDA. FDA described the assumptions FDA made to estimate the costs of the proposals. Instead of forming separate working groups, FDA and Industry held several working discussions of the details of the proposals during this negotiation meeting. FDA and Industry agreed to continue working discussions during the next negotiation meeting.

FDA's Cost Estimate of Industry Proposal

FDA developed cost estimates based on analysis of materials from Industry's November 18, 2015, presentations and subsequent discussions with Industry on December 15, 2015. For each proposal element, FDA estimated costs based on the agency's assumptions of workload and associated resources, and target performance levels that FDA believes are feasible. FDA used professional judgment based on past experience and program knowledge to suggest feasible performance ramp-ups.

FDA provided a summary of the agency's cost estimate for Industry's proposal, followed by detailed discussions of the assumptions for each component. FDA estimated that the additional resources to implement Industry proposals over the five-year authorization period of MDUFA IV would total $456.4 million, in addition to the amount of user fees needed to maintain the level of staffing and other activities supported by MDUFA III user fees. FDA noted that these estimates do not contain inflation adjustments.

Industry's Process Improvement and Independent Assessment Proposals

During the November 18 negotiation meeting, Industry proposed several ideas intended to improve the efficiency of the review process, including tracing deficiencies to specific references and providing the sponsor immediate access to review summaries; supervisory oversight enhancements for certain milestones or processes, including new data requests, communications that impact the review clock, withdrawals, and conversions from Special 510(k) submissions to Traditional 510(k)s; training on review of submissions for modifications; exploring an IT link of Pre-Submissions to subsequent submissions and enhanced tracking of submission types, including LDT tracking; and allowing for transition periods for new standards/guidance documents.

To provide a cost estimate for these process improvement proposals, FDA excluded the proposal for access to review summaries, which was analyzed separately. FDA determined that most of the remaining proposals could be addressed through FDA's Review Process Infrastructure enhancements proposed on December 15, 2015. FDA determined that the proposal for improved supervisory oversight of new data requests, communications impacting the review clock, withdrawals, and conversions from Special 510(k) submissions to Traditional 510(k)s could be covered as part of the Review Process Infrastructure enhancements by increasing the number of review managers to reduce the reviewer-to-manager ratio to improve oversight and consistency of review activities as proposed by Industry. FDA determined that a Quality Management Team established under the Review Process Infrastructure enhancements could address industry's request for tracing deficiencies to specific references through audits of deficiencies to ensure clear rationale for identified deficiencies. FDA further determined that the proposal for IT linkage of pre-submission to subsequent submissions and the proposal for enhanced tracking of submission types, including LDT tracking, could be accomplished through the FDA MyDevice/eSubmitter proposal, which is also part of the agency's Review Process Infrastructure enhancement proposal. Finally, after further clarification from Industry, FDA determined that the proposal for training on review of submissions for modifications could be covered as part of the Review Process Infrastructure enhancements as well. FDA estimated the cost for the Review Process Infrastructure improvements to be 46 FTEs, including targeted recruitment specialists, review managers, and a Quality Management team.

AdvaMed, MDMA and MITA also proposed to continue the Independent Assessment. FDA estimated $3 million in contract obligations to conduct targeted assessments of identified aspects of the Medical Device Program. FDA noted that the FDA effort for implementation would be covered by FTEs included in the Review Process Infrastructure enhancements. The total special operating costs over the five years of MDUFA IV to implement the proposed review process improvements and continue the Independent Assessment was estimated to be $22.5 million, including a one-time $6.5 million in start up costs for MyDevices/eSubmitter, $2.5 million in annual IT costs, and $1.7 million each year in proposed management incentive pay. This total also accounts for efficiencies of up to $2.0 million annually by reducing the FDA Document Control Center contract as myDevices/eSubmitter is phased in.

Industry's Review Summaries Proposal

During the November negotiation meeting, AdvaMed, MDMA and MITA proposed that FDA provide the sponsor immediate access to review summaries. To determine the cost of this proposal, FDA focused on the perceived intent of the proposal as described by industry, which is to provide insight into the review process and aid in future submission preparation. FDA's cost estimate is based on the following assumptions: review summaries would be provided for all 510(k) submissions that receive a MDUFA decision (3200 submission volume); the review summary would be provided directly to the 510(k) sponsor immediately following the MDUFA decision; the lead reviewer would prepare the review summary; and the content would be based

on the lead reviewer's memo, redacted for proprietary or confidential commercial information (CCI) and privileged deliberative information. FDA estimated the resulting additional workload, and assumed that all review staff would require Freedom of Information Act (FOIA) training to be able to identify CCI content that should be redacted from the review summary and the review summaries would be reviewed by FOI staff prior to release. FDA estimated the cost of this proposal to be 42 FTEs and $1.5 million in training costs.

ACLA asked if the cost for the review summaries proposal includes any assumptions for incremental increases in submissions for Laboratory Developed Tests (LDTs). FDA clarified that the scope of the estimate was limited to devices currently regulated by the Office of Device Evaluation (ODE) and the Office of In Vitro Diagnostics and Radiological Health (OIR) and did not include any assumptions regarding LDTs. FDA further clarified that the assumed submission volume for review summaries was limited to devices that currently do not receive review summaries (i.e., the estimate excluded the volume of review summaries currently provided for in vitro diagnostic devices). FDA noted that the possibility of workload increases warrants further discussion of a mechanism to address workload uncertainty.

FDA and Industry discussed the details of this proposal and compared it to OIR's process for providing publicly available review summaries for 510(k)submissions. Industry noted that they may be willing to consider alternatives that allow for a longer timeline for providing access to review summaries after the final decision (rather than "immediate" access), as well as options for reducing the number of 510(k)s subject to this process (by excluding certain types that are less complex). Industry also noted that this process also could apply to PMA supplements.

Industry's Pre-Submission Proposal

During the November negotiation meeting, AdvaMed, MDMA and MITA proposed that the Pre-Submission meeting should be scheduled within 60 days of the request with a goal of 90% achievement. They further proposed that pre-meeting feedback should be sent to the Sponsor at least 4 business days prior to the meeting for 98% of meetings. In addition, they proposed that there should be greater consistency regarding the granting of longer meetings and that there should be a clear policy describing the circumstances under which sponsors with complex submissions should be granted meetings that last longer than one hour. They also expressed a desire for a mechanism for communication on missed goals for scheduling Pre-Submission meetings and pre-meeting feedback.

To determine the cost of this proposal, FDA followed Industry's estimates for the Pre-Submission volume to level off. However, FDA noted that a workload uncertainty mechanism should be used to ensure resources are proportional to actual workload if this assumption does not hold over the five years of MDUFA IV. ACLA noted that in the event LDTs are regulated by FDA, the volume of Pre-Submissions could increase significantly. FDA further assumed that the review effort associated with longer meeting times will be offset by a corresponding reduction in volume. FDA noted that according to the previously described proposal to decrease

the reviewer-to-manager ratio as part of the Review Process Infrastructure enhancements, there would be increased availability of managers to attend longer meetings. To implement the proposal from AdvaMed, MDMA and MITA, FDA estimated a cost of 57 FTEs and $0.6 million annually in IT costs. FDA described the performance goals for this cost estimate, which allow for a performance ramp up to industry's proposed performance goals by the third year of MDUFA IV (FY20). FDA noted that this revised performance ramp up is as fast as logistically feasible.

Industry asked clarifying questions on the difference between Pre-Submissions and Q-Submissions. FDA clarified that Pre-Submissions are a subset of Q-Submissions; the latter also include other subsets, such as informational meetings and submission issue meetings.

Industry's PMA Proposal

AdvaMed, MDMA and MITA proposed the adoption of goals for additional milestones for the review of PMAs beyond those agreed to in MDUFA III. They proposed that Good Manufacturing Practice (GMP) inspections be conducted 60 days prior to the FDA decision. In response to this proposal, FDA provided the numbers of Approvable Pending GMP (AGMP) decisions in the 2014 and 2015 decision cohort, totaling 9 AGMP decisions. From their analysis, FDA determined that scheduling and conducting an inspection sooner may allow industry the opportunity to address compliance and device review issues concurrently, thereby reducing the issuance of AGMP letters. In order to address industry's proposal, FDA proposed that by day 30, the initial desk review of the manufacturing module of a PMA would be complete and domestic inspections would be conducted at least 60 days prior to the MDUFA decision (i.e., by day 120). FDA did not include in its proposal PMAs requiring foreign inspections, PMAs for combination products, situations in which the sponsor is not ready for an inspection at the time of scheduling, or situations in which a second inspection is required. FDA estimated 33 FTEs and a total of $150,000 in IT operating costs to implement this proposal, assuming a PMA volume of 43 submissions.

FDA noted that it is the Sponsor's responsibility to respond to any deficiencies within 30 days of the inspection. Industry agreed that it is a shared responsibility between FDA and the Sponsor and noted that there may be a need to educate some Sponsors on their responsibilities. Industry discussed if this performance goal would apply to original PMAs, Panel-Track Supplements, and 180-day Supplements. Industry also raised concerns on the timing of Bioresearch Monitoring (BIMO) inspections, and FDA agreed to discuss this further.

Industry clarified that their PMA proposal was also intended to address Approvable pending resolution of minor deficiencies (ADEF) decisions, in addition to AGMP decisions. FDA did not consider ADEF decisions in estimating the cost of this proposal. FDA agreed to consider these decisions for future discussions and noted that only 7 ADEF decisions were issued in 2013 and 2014. FDA noted that these decisions are most often due to labeling or Post-Approval Study

deficiencies. Industry raised the possibility of addressing the ADEF decisions through Interactive Review, but FDA noted that the deficiencies are not always easily resolved.

AdvaMed, MDMA and MITA further proposed a goal of 90% of PMA Approval orders issued within 60 days of an Approvable decision. FDA noted that they cannot commit to a performance goal structured around committing to issue an "Approval" decision because the decision is contingent on the sponsor's ability to resolve the issues identified. FDA and Industry discussed alternative ways of addressing the underlying concern, such as providing a plan for resolving outstanding issues that includes responsibilities and target timelines, similar to the "missed MDUFA decision" plans implemented for 510(k) and PMA submissions under MDUFA III.

AdvaMed, MDMA and MITA also proposed that for 90% of submissions with a panel meeting the FDA decision be issued within 60 days of the panel meeting. FDA proposed several process changes to address this goal to create shared efficiency between industry and FDA. FDA described a proposed schedule for FDA and industry to meet, discuss, and resolve remaining issues (e.g., relating to labeling, SSED document, and post approval studies) within 40 days post-panel meeting. To determine the cost of this proposal, FDA assumed that all review staff assigned to the PMA would spend more time on the PMA in the 60 days following the panel meeting. FDA estimated the cost to be 27 FTEs and $200,000 in IT modifications, assuming the FY14 workload of 6 panel meetings per year is constant. Industry discussed concerns on the variation in number of calendar days from panel meeting to decision and agreed to further discussions to fine tune the approach to address the issues they raised with this proposal.

Industry's De Novo Proposal

AdvaMed, MDMA and MITA proposed new goals for the review of *de novo* requests, including a proposal for 90% of direct *de novos* to receive a decision in 120 days, while 90% of post-not-substantially-equivalent (post-NSE) decision *de novos* would receive a decision in 90 days. In order to determine the cost of this proposal, FDA assumed that the number of *de novo* requests would increase to 72 in FY17 and remain constant throughout MDUFA IV. FDA did not provide an estimate of resources for improving performance of post-NSE decision *de novos*, noting that the number of post-NSE de novo submissions has fallen to just one in FY15, hence the additional IT cost to track this performance goal would not be cost-effective. FDA noted that it is not practical to commit to a 90% performance goal in the first year of MDUFA IV, due to current performance levels, necessary training, and onboarding limitations. To estimate the cost of Industry's proposal, FDA assumed that the 90% performance goal would be reached by Year 4 of MDUFA IV. Given the significant improvement in performance necessary to reach the requested 90% performance goal, FDA estimated the cost of this proposal to be 100 FTEs and $200,000 annually in IT costs.

Industry raised questions on the range in complexity of *de novo* requests and the workload for reviewers. FDA explained there is a wide variety of requests, with a range of risks and indications. FDA further explained that the *de novo* is a classification process that involves many

considerations and steps. FDA raised the possibility of having a Refuse-to-Accept (RTA) policy and a goal for Substantive Interaction on *de novo* requests. Industry agreed to discuss these possibilities further.

Industry's CLIA Proposal

AdvaMed, MDMA and MITA proposed goals for the review of Clinical Laboratory Improvement Amendments (CLIA) waivers intended to achieve greater predictability, timeliness, and clarity on the review of these submissions. The proposed goals include a 95% goal to receive a decision in 90 days on CLIA waiver by application single submissions without a panel meeting, a 95% goal to receive a decision in 120 days on CLIA dual 510(k) / waiver by application submissions without a panel meeting, and a 95% goal to receive a decision in 320 days on CLIA waiver submissions with a panel meeting. FDA provided a cost estimate for the proposal, while noting that FDA's initial analysis indicates that there could be legal impediments to FDA using MDUFA funds to implement industry's CLIA proposal. FDA and Industry agreed that further legal analysis is needed before proceeding with this proposal.

Industry asked clarifying questions on the cost estimate for the CLIA proposal and discussed the current quality of CLIA Waiver applications.

Discussion

During the December negotiation meeting, FDA and Industry discussed the possibility of establishing working groups to address technical details for several of the proposals. FDA and Industry discussed the details of each proposal's cost estimates during the negotiation meeting. FDA and Industry utilized these working discussions to form a greater understanding of the proposals without breaking into separate working groups. Industry inquired whether FDA had considered within its resource estimates opportunities for resource and cost efficiencies. Further, industry asked FDA to evaluate whether the projected amount of resources and FTEs would still be needed once the proposed IT systems and process improvements are implemented. FDA and Industry have agreed to continue these working discussions during the upcoming negotiation meetings.

FDA noted that there may be other approaches to addressing the proposals from Industry that may provide a more attractive balance of cost versus performance. FDA and Industry agreed to continue discussion of alternative approaches at the next negotiation meeting.

Next Meeting

The next meeting is scheduled on January 27, 2016.

Meeting End Time: 3:45 pm