FDA – Industry MDUFA IV Reauthorization Meeting
November 18, 2015, 9:45 am – 3:45 pm
FDA White Oak Building 66, Silver Spring, MD
Room 4404

Purpose

To discuss 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)
Toby Lowe	CDRH
Thinh Nguyen	Office of Combination Products (OCP)
Brendan O'Leary	CDRH (SME)
Geeta Pamidimukkala	CDRH
Prakash Rath	Office of Legislation (OL)
Don St. Pierre	CDRH
Darian Tarver	OC
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)
Elisabeth George	Philips (representing MITA)
Allison Giles	Cook (representing MDMA)
Mark Gordon	Abbott (representing AdvaMed)
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)
John Manthei	Latham & Watkins (representing 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 November user fee negotiation meeting, FDA and Industry presented their respective initial proposal packages for MDUFA IV. FDA and Industry acknowledged commonality around the themes of consistency and predictability in the medical device review program, as well as process improvements that include pre-submission consultations and *de novo* submissions. The parties also noted some apparent differences in the approaches taken to address the common themes. FDA and Industry anticipate productive discussions on the details of and assumptions underlying the proposal packages.

Overview of FDA Proposals

FDA opened the negotiation meeting by identifying important areas of agreement between FDA and Industry: improvements to the medical device review program in MDUFA IV should build on the successes of MDUFA III; improve the consistency, predictability, and transparency of the review process, in line with the recommendations of the Booz Allen Hamilton (BAH) Independent Assessment; improve the efficiency of the review process; and, continue to reduce total time to decisions. FDA emphasized that it has demonstrated commitment to the success of the program by meeting goals, being more interactive and transparent, and striving to make further improvements during MDUFA III. FDA noted that in addition to the successes achieved in MDUFA III, there remain areas of vulnerability and opportunity, such as increasing workload, management systems and infrastructure, recruiting and retention, and the increasing pace of innovation. FDA described the need to finish building the program, beyond the investments from MDUFA III, to further improve the program and take advantage of the momentum to put the program on a healthy and sustainable path for the future.

FDA noted that much of the proposal package is framed around the Independent Assessment recommendations to improve consistency. The investments in MDUFA III were focused on timely decisions in all review branches, and MDUFA IV presents an opportunity to extend

beyond simply on-time performance to include more quality and consistency in decision making across all review branches.

FDA stated its belief that the proposal package is a good investment that will establish a more consistent, predictable, transparent, and efficient program that benefits all companies. FDA provided initial resource estimates for the main components of the proposal package, noting that there are many assumptions that will need to be discussed with Industry before a more detailed overall estimate of costs can be assembled. FDA also discussed the need for a mechanism for accounting for changes in workload to ensure that resources are sufficient to attain performance goals if workload exceeds projections.

Ensuring Consistent, Predictable, and Efficient Review Experience

FDA presented several opportunities for improvement in MDUFA IV with proposals focused on ensuring a consistent, predictable, and efficient review experience.

Quality Management System

FDA proposed the establishment of a robust overarching Quality Management (QM) System for the premarket review process, using the BAH recommendations and other appropriate standards as a guide. The proposed QM team responsibilities would include systematic audits of consistency in areas such as pre-submissions and cross-cutting scientific areas. The proposed QM team would develop, monitor, and maintain quality metrics through a program management dashboard. The QM team would measure the impact of Corrective and Preventive Action (CAPA) and Continuous Process Improvement (CPI) activities and new policies, programs, and review tools. Under this proposal, the QM team would also be responsible for document control, knowledge management, CAPA investigations, and FEEDBACK CDRH, in addition to coordinating future independent assessments or external audits.

The proposed QM System would rely on modern tools that enable electronic submissions, Industry tracking of their submission status while under review, and enhanced FDA program audits. FDA described the myDevices portal, which would accept structured data that is immediately uploaded into FDA's database, resulting in time savings, efficiency, and consistency for both FDA and Industry. Complete submissions would reach reviewers faster and Industry could view real-time submission status throughout the process. FDA explained that myDevices has features beyond submission tracking; it can be used as an electronic submissions gateway through which sponsors can submit structured data sets, which would greatly enhance FDA's capability to manage information and enable more robust audits and analysis of performance.

Recruitment, Retention, and Development of Managers and Staff

FDA highlighted the need for consistency through managerial oversight and enhanced recruiting. FDA proposed to decrease the reviewer-to-manager ratio from an average of approximately 11:1 to 8:1 to ensure managers have the opportunity to provide adequate oversight of the review process and review decisions. FDA further proposed a tiered retention allowance for supervisors, which would provide incentive pay to attract and maintain talent in managerial positions. FDA also proposed to incorporate targeted scientific and technical expertise into an enhanced recruitment and hiring process.

Program Reliability, Resiliency, and Transparency

FDA presented proposals for improving the performance of the review process. The MDUFA IV proposal package includes maintenance of the MDUFA III FDA performance targets for 510(k) and PMA submissions and expands performance goals to other premarket processes, including *de novo* submissions, Pre-Submissions, Submission Issue Meetings (SIMs), and Third Party 510(k) reviews.

FDA described the upward trend in number of *de novo* requests, for which FDA is expending increasing effort to review. Due to the increased workload and limited resources, FDA is currently meeting the 120 day target for only approximately 40% of *de novo* requests. FDA proposed that user fees be provided to increase review capacity such that 70% of *de novos* can be completed within 120 days by the end of MDUFA IV.

FDA also described the Pre-Submission program, which has also experienced a steadily increasing workload. During MDUFA III, FDA has used efficiencies gained from changes to other program areas to dedicate additional FTE to the review of all Q-Submissions (which include Pre-Submissions and other types of FDA feedback) compared to the staff dedicated to Pre-IDEs prior to MDUFA III. FDA believes this program has value and is concerned that continuation of the program “as resources permit” may negatively affect the program. Therefore, FDA proposed that user fees be provided to increase review capacity such that 95% of Pre-Submissions can be completed within 60 days by the end of MDUFA IV.

FDA noted that, similar to Pre-Submissions, the third party 510(k) review program is operated “as resources permit” under MDUFA III. Based on increasing review times and a sharp decline in use of the program, FDA believes a course correction is needed. A recent survey of FDA staff who assessed 510(k)s reviewed by third parties indicates that 80% of such submissions had major issues in 5 key areas, including not providing a substantial equivalence rationale, not providing a summary of the review, and not providing a comparison to the predicate device. FDA proposed a multi-pronged approach to address the third party review program by training third parties, providing redacted example reviews, auditing third parties, tracking the scientific quality of the review memos, removing incompetent third parties, and tailoring the program for specific, targeted areas. With dedicated resources to correct and maintain oversight of the

program, FDA proposed to make a decision on 85% of Third Party 510(k)s within 30 days by the end of MDUFA IV.

For 510(k)s not reviewed by third parties, FDA reported the average total time to decision, for which there has been a reduction since 2010, has been largely driven by a reduction in manufacturer time. FDA attributes this change to increased interactions between FDA and Industry to quickly resolve issues on the FDA clock, with fewer and shorter hold times. FDA pointed to the simultaneous increase in 510(k) substantially equivalent decisions as evidence that issues are being resolved. FDA proposes to build on the BAH recommendations for increased interactive review (IR) by increasing the use of IR earlier in the review process. FDA expects that this will lead to fewer holds and a continued decrease in total time to decision of an average of 10 days by the end of MDUFA IV. FDA noted that this process is more resource intensive and requires additional reviewers to create additional capacity to maintain performance, yet the benefit to Industry is faster resolution of submission issues, and therefore reduced total time to decision.

After describing these specific opportunities for improvement, FDA summarized the review process proposals that are intended to target the entire process for the review of device applications. FDA proposed to establish performance goals and to shorten time to feedback for Pre-Submission review. FDA further proposed to reduce the Refuse-to-Accept (RTA) rate and to automate acceptance review using the myDevices tool. During the substantive review phase, FDA proposed to increase the use of IR, add a Substantive Interaction (SI) goal for *de novos*, and maintain all other SI goals from MDUFA III. If the proposal were to be implemented, FDA would expect the need for SIMs to reduce due to the increased use of IR during the substantive review phase. For the remaining SIMs, FDA proposed to provide timely feedback by establishing performance goals for their review. FDA proposed to add decision goals for *de novos* and third party reviews of 510(k) applications, and to reduce the total time to decision for 510(k) applications. For submissions for which FDA proposed to add performance goals, FDA proposed to improve performance over the previous year throughout the five years of MDUFA IV.

FDA reiterated that these proposals can enable more timely access to safe, effective, and innovative devices for patients. Investing in these proposals would result in more consistent decision-making, more timely interactions, more timely decisions, and improved transparency.

Innovative Review Process for Innovative Products

FDA proposed several ideas intended to keep pace with rapid changes in medical device technology and regulation. One proposal would expand the use of patient preference information (PPI) in the determination of a device's benefits and risks. FDA described patient preference information as an understanding of the risks patients are willing to accept to get the benefits of a device. FDA explained that because PPI factors into the benefit/risk profile of a device, it can be

used to support approval or clearance of a device when other data may suggest taking another approach, such as FDA requesting additional data or not approving or clearing the device. Because FDA has few staff with the expertise needed to review PPI, FDA proposed using user fees to pay for staff to review PPI when it is included in a submission and to help sponsors determine the best methods for collecting PPI. This staff group would be available for internal and external consultations on submissions to determine how patient input factors into the benefit/risk determination. FDA's proposal also included resources for training and to support consortia to develop less burdensome frameworks and tools to support the use of PPI.

FDA also proposed to expand the use of evidence from clinical experience by hiring staff and investing in a system to link data from health care claims, electronic health records, and registries. FDA explained that much of that data is already being collected as part of routine clinical care but it exists in silos; linking the various sources could create a network of data to support premarket decision making. FDA forecasts potential benefits may include fewer standalone clinical trials, shorter or smaller clinical trials because of more efficient enrollment, easier patient follow-up, and harmonization with other national and international data. Using evidence from clinical experience would also allow greater use of shifting data from the premarket to postmarket setting, which would allow patients earlier access to devices while collecting information to validate the device's safety and effectiveness or substantial equivalence or to support expanded use. FDA explained that another benefit is the potential obviation of post-approval studies because data about a device's use or performance could be gleaned from the system linking data from registries, claims, and electronic health records. FDA's proposal includes staff to develop a framework to define how registries can be qualified and used for premarket review, to link data from claims and registries, and to set up registries to support premarket decision making, as well as resources to support infrastructure development.

Another proposal to support innovation is FDA's lifecycle coordinated approach to software and digital health device regulation to focus resources where they will most benefit public health. FDA noted the need for smart policy on areas of interoperability, clinical decision support, software modifications, telemedicine, and cybersecurity. FDA described a need for additional resources for training, oversight, public engagement, and IT to support and improve submission tracking. FDA proposed additional staff who would streamline and align FDA processes with software lifecycles and increase the number of software experts available to develop policy and to review devices containing software to ensure consistent approaches across the Center. FDA also proposed additional resources for IT to support and improve submission tracking.

In response to feedback from AdvaMed, MITA and MDMA on the need for more device-specific guidance documents, FDA proposed to focus on ensuring timely development of device-specific guidance documents. FDA proposed to establish a new guidance model for streamlining device-specific guidance documents, increasing the number of such guidance documents, and ensuring they are finalized in a timely manner. FDA noted the importance of ensuring current final guidance documents remain relevant and up-to-date and described a current lack of

resources to accomplish this. FDA stated that its proposal would provide more transparency and predictability for devices to get to market.

FDA proposed to establish a mechanism through which FDA would not review test results demonstrating conformance to certain standards if those results were certified by an accredited test lab. FDA would review currently recognized standards to identify those most appropriate for such a mechanism. FDA noted this proposal would minimize redundancy and testing, and that the expectations for test results would be very clear. FDA proposed additional staff and resources to develop and implement the performance scheme, develop associated guidance documents, hold a public workshop, develop appropriate IT infrastructure, and training.

FDA presented its arguments for the need to add a workload adjustment mechanism to the MDUFA framework. Currently there is no mechanism for FDA to receive additional user fees if submission volumes and their associated workload increase, which FDA stated would put at risk its ability to achieve the performance goals. Moreover, the current user fee offset provision requires FDA to reduce fees in the final year of the 5-year authorization period when collections in the prior years exceed the total authorized 5-year amount, even if those over-collections reflect submission fees that generate increased workload. FDA stated that a workload adjustment mechanism would also enable FDA to accommodate potential changes in submission volumes due to uncertainties with pending legislation, laboratory developed tests (LDTs) that may be subject to premarket review, the volume of 510(k) submissions reviewed by third parties, and the actual number of de novos and pre-submissions, which have been increasing but may level out at some point.

FDA summarized by noting that the proposals are intended to strengthen the existing device review program and that all companies benefit from having a more consistent and predictable review experience, shorter total time to decision, tools to facilitate good communication, and quality service. FDA concluded by reiterating the common goal of getting high quality, safe, and effective devices to patients first in the world, and expressed confidence that FDA and Industry could develop successful solutions for improving the program.

MDUFA IV Proposal Presented by AdvaMed, MDMA, and MITA

AdvaMed, MDMA, and MITA reiterated their support for the CDRH vision for patients in the U.S. to have access to high-quality, safe, and effective medical devices first in the world. They noted the progress achieved under MDUFA III and the opportunities to improve reasonableness, accountability, and consistency of the program. They also noted that the Booz Allen Hamilton (BAH) report offered tangible, meaningful best practices that they incorporated into their proposal presentation. Their objective for the program is to improve the predictability and quality of the experience, which will have the effect of improving review times. Their motivations for their proposals include avoiding significant changes to the goal structure developed in MDUFA III; refining targeted programs that focus on predictability, transparency,

and accountability; developing goals for certain submission types; and, focusing on discrete process improvements to facilitate communication. They noted that they recently requested additional data from FDA to support further development of one proposal.

Pre-Submission process

The proposal of AdvaMed, MDMA and MITA on the Pre-Submission process, which they noted is highly utilized, is intended to address perceived inconsistencies and lack of clarity regarding granting longer meetings and to provide greater value through consistent, predictable, and timely scheduling of Pre-Submission meetings and pre-meeting feedback. They 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 4 business days prior to the meeting for 98% of meetings. In addition, they proposed that 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. They proposed that FDA update and provide training on the Pre-Submission guidance to reflect these pieces of their proposal.

Adoption of goals for additional submission types and key milestones

AdvaMed, MDMA and MITA presented a proposal for the adoption of goals for additional submission types and milestones beyond those agreed to in MDUFA III. Two issues that this proposal is intended to address are (a) the time period between a PMA Approvable decision and the issuance of the Approval order, and (b) the time period from a panel meeting until an FDA decision on a PMA. They proposed to address these issues through a goal of 90% of PMA orders issued within 60 days of an Approvable decision. In addition, they proposed that Good Manufacturing Practice (GMP) inspections be conducted 60 days prior to the FDA decision. They also proposed that for 90% of submissions with a panel meeting the FDA decision be issued within 60 days of the panel meeting.

AdvaMed, MDMA and MITA further proposed new goals for the review of *de novo* requests to address inconsistent review times and to avoid growing disparity as other premarket review submissions are subject to tighter goals under MDUFA III. They proposed that 90% of direct *de novos* receive a decision in 120 days, while 90% of post-not-substantially-equivalent (post-NSE) decision *de novos* receive a decision in 90 days.

AdvaMed, MDMA and MITA also 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 single submissions without a panel meeting, a 95% goal to receive a decision in 120 days on CLIA waiver dual submissions without a panel meeting, and a 95% goal to receive a decision in 320 days on CLIA waiver submissions with a panel meeting. They noted that these goals represent improvements over the current goals

for these submissions, which are important for the public health because they allow point-of-care tests in clinical environments. They also noted their desire for a "no submission left behind" mechanism for CLIA submissions.

In addition to the specific goals presented in this proposal, AdvaMed, MDMA and MITA also expressed a desire to discuss the development of goals for 513(g) requests for classification, and distinguishing between the performance of Special and Traditional 510(k) submissions. They stated that additional data would be necessary to develop an appropriate goal structure for these submission types.

Continuation of Independent Assessment

AdvaMed, MDMA and MITA expressed support for a continuation of the Independent Assessment. They proposed that FDA implement the corrective action plan that was developed in response to BAH recommendations. They further proposed that FDA incorporate more accountability and improved metrics to assess performance to minimize variation among reviewers and branches. The proposal also called for the implementation of a robust CAPA system, training on the submission assignment process and workload distribution, and an analysis of the conversion rate of Special 510(k) submissions to Traditional 510(k) submissions.

Process Improvements

Finally, AdvaMed, MDMA and MITA proposed several ideas intended to improve the efficiency of the review process. Ideas included tracing deficiencies to specific references and providing the sponsor 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, allowing for transition periods for new standards/guidance documents.

ACLA Presentation on MDUFA IV LDT-Related Proposals

ACLA restated its position that LDTs are not medical devices under the Federal Food, Drug, and Cosmetic Act. To the extent that LDTs are regulated as medical devices within MDUFA IV, ACLA proposed that FDA should add a field in the Agency's relevant databases that would enable the data to be reported separately for LDTs, and report key metrics with a separate line comparing IVDs to LDTs. ACLA specifically requested that the Commitment Letter state that FDA will treat LDTs no less favorably than other regulated items at CDRH.

Discussion

FDA and Industry discussed their initial questions and observations on the proposal packages.

When asked by Industry, FDA clarified that the proposal for systematic audits of cross-cutting scientific areas would consist of dedicated resources to audit specific areas of review, such as the review of electromagnetic compatibility (EMC) or biocompatibility and the variability of questions asked during a review.

Industry clarified that they intend their proposed performance goals to take effect in the first year of MDUFA IV. FDA asked AdvaMed, MDMA and MITA to further describe their proposal to ensure no Pre-Submissions miss performance goals. They explained that the purpose is to have appropriate communication so meetings get scheduled and feedback is received in a timely manner. If the pre-meeting feedback is not received 4 days prior to the meeting, they would like to receive some communication from FDA. On the topic of Pre-Submissions, FDA discussed with AdvaMed, MDMA and MITA the reasons a Pre-Submission meeting might be longer than one hour. AdvaMed, MDMA and MITA agreed to provide examples of different experiences with Pre-Submission meeting length. FDA also asked AdvaMed, MDMA and MITA for more clarity on their proposal to put goals on the timeframe for an approvable decision and how this may relate to the scheduling of GMP inspections. During this discussion, FDA noted that this could be one of several process improvements addressed by adopting a Total Product Life Cycle (TPLC) approach for devices reviewed by the Office of Device Evaluation (ODE), similar to the approach used by the Office of In Vitro Diagnostics and Radiological Health.

FDA agreed to work on an initial estimate on the resources to accomplish the goals and commitments indicated in Industry's proposal package, with the goal of completing that by the next negotiation meeting. FDA and Industry agreed to postpone the demonstration of the MyDevices interface until the next meeting. To facilitate discussion at the next meeting, both parties agreed to exchange written questions on the proposals by December 8, with possible additional questions by December 11.

Next Meeting

The next meeting is scheduled on December 15, 2015.

Meeting End Time: 3:45 pm