Minutes From Negotiation Meeting on MDUFA III Reauthorization, October 21, 2011

U.S. Food & Drug Administration

FDA - Industry MDUFA III Reauthorization Meeting
October 21, 2011, 10:20 am - 5:00 pm
FDA White Oak Building 1, Silver Spring, MD
Room 2102

Purpose

To discuss MDUFA III reauthorization.

Participants

FDA

Malcolm Bertoni	Office of the Commissioner (OC)
Nathan Brown	Office of Chief Counsel (OCC)
Kate Cook	Center for Biologics Evaluation and Research (CBER)
Christy Foreman	Center for Devices and Radiological Health (CDRH)
Bill Hubbard	FDA Consultant
Elizabeth Hillebrenner	CDRH
Toby Lowe	CDRH
Thinh Nguyen	CDRH
Tracy Phillips	CDRH
Don St. Pierre	CDRH
Francisco Vicenty	CDRH
Nicole Wolanski	CDRH
Barbara Zimmerman	CDRH

Industry

Susan Alpert	Medtronic (representing AdvaMed)
David Fisher	Medical Imaging Technology Alliance
John Ford	Abbott Laboratories (representing AdvaMed)
Elisabeth George (ph)	Phillips (representing (MITA)
Donald Horton	Laboratory Corporation of America Holdings (representing ACLA)
Mark Leahey	Medical Device Manufacturers Association
James Ruger	Quest Diagnostics (representing ACLA)

Patricia Shrader	Medtronic (representing AdvaMed)
Janet Trunzo	Advanced Medical Technology Association

Meeting Start Time: 10:20 am

FDA provided a response and counter-proposal to the proposal offered by Industry[1] [1] on October 6, 2011.

Product Development Goals

Industry's October 6, 2011 proposal allows applicants 15 days to draft pre-submission meeting minutes followed by 15 days for FDA to provide edits to the applicant's draft minutes and 15 days for the applicant to indicate disagreement with how a significant issue or action item has been documented. If disagreement is noted, a teleconference would be held during the 15-day period and FDA would finalize minutes within 15 days of the teleconference. At FDA's request, Industry confirmed that scheduling the teleconference within the 15-day period described above is the expectation; however, scheduling problems may result in some teleconferences beyond the 15-day target.

On October 6, 2011 Industry proposed that "modifications to FDA's feedback will be limited to situations in which FDA has concluded that the feedback does not adequately address important new issues materially affecting safety or effectiveness." FDA re-stated its concern with the characterization of such issues as "new," noting that there may be rare occasions in which FDA subsequently discovers something materially relevant to safety and effectiveness that potentially could have been identified earlier; on these rare occasions, FDA must raise the issue in the interest of public health. Industry clarified that they are not seeking to limit FDA's ability to request material information regarding safety and effectiveness, but rather to limit "nice to know" requests, particularly from reviewers new to the device/submission. Industry and FDA agreed to add a statement to the beginning of the Commitment Letter confirming that nothing in the commitment letter precludes the Agency from exercising its authority to assure the safety and effectiveness of medical devices.

FDA and Industry agreed that pre-submission goals and the number of submissions to which the quantitative pre-submission goal applies may be reevaluated as part of the financial discussions, as the ability of the Agency to meet the timeframes proposed may be affected if the number of pre-submission requests exceeds assumptions.

Performance Goals

Industry stated its concern that FDA may limit applicant time to respond to Additional Information requests and Major Deficiency Letters in order to achieve quantitative total time performance goals. FDA stated its intent to follow current guidance on extensions as outlined in the following guidance documents: "FDA and Industry Actions on Premarket Notifications (510(k)) Submissions: Effect on FDA

Review Clock and Performance Assessment" and in "FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals." FDA confirmed that the time allotted to applicants for responding will not be less than outlined in the above guidance documents. FDA also plans to ask applicants for reasons why applicants are requesting extensions. Such data will be analyzed to guide program improvements but will not be used as a basis to reject extensions requests.

FDA proposed quantitative goals for substantive interactions and one-tier MDUFA decision goals for Original PMAs, PMA Modules, 180 Day PMA Supplements, Real-Time PMA Supplements, and 510(k)s. The goals establish specified review time targets, which progressively apply to greater percentages of submissions over the course of MDUFA III. The purpose of the progressive goal structure is to establish achievable performance in the first year of MDUFA III, and to reflect the time needed to hire and train new reviewers prior to reaching the ultimate performance targets that exceed the current MDUFA II performance levels. There was discussion as to whether the initial year goals should begin with current performance or current MDUFA II goals. Setting initial goals based on historical performance or MDUFA II goals is complicated by the creation of new goals for substantive interactions, creation of new PMA cohorts based on the need for Advisory Committee input, and inability to predict the exact impact of new pre-submission goals and Refuse to Accept (RTA) and Refuse to File (RTF) policies on review times. Additionally, FDA considered the review system as a whole and attempted to balance concerns about improved performance with concerns about the increase in resources needed to achieve improvements. FDA attempted to identify specific areas that Industry had identified as priorities, and to prioritize additional resources to those areas rather than propose goals that did not provide value commensurate with the incremental increase in resources that would be required to meet them. For example, FDA understood from Industry that timely decisions on marketing applications are most important. In its proposal, FDA therefore focused less priority on improvements in the timely review of PMA modules in favor of improvements to timely review of marketing applications. Industry noted concern with any interim goal that suggests a reduction in current performance or MDUFA II goals, requested additional data on current performance, and suggested additional discussion would be necessary in some areas of FDA's proposal.

FDA further clarified the proposed tailored communication on all Original PMAs and 510(k)s that miss the one-tier goal. FDA explained that the communication would include the outstanding issues preventing FDA from reaching a decision, and action items for both parties with an estimated date for completion. Industry inquired as to how this differs from current practice. FDA explained that currently there is no policy or common practice of systematically communicating with an applicant after a goal is missed. Under the current two-tier system, when a Tier 1 goal is missed the tracking system calculates the Tier 2 goal and the submission typically is lowered in the reviewer's work queue. When a Tier 2 goal is missed, Office leadership discusses the submission with the review Division, but the applicant is not necessarily provided an update as to the status of the application. Industry suggested additional clarification to FDA's proposal.

While FDA has proposed eliminating Tier 2 goals, FDA stated it is their belief and expectation that FDA performance at 150 review days will be improved for 510(k)s under the proposed goal structure.

FDA proposed extension of the PMA review clock by 100 FDA days upon submission of an unsolicited major amendment, noting that a consistent approach would be easier to manage than the current formula used in MDUFA II. Industry indicated a concern that submission of an unsolicited major amendment prior to day 135 would be penalized when compared to MDUFA II practices. FDA explained that most unsolicited major amendments are submitted later in the review process. Industry requested data on the number and timing of unsolicited major amendments.

FDA proposed a separate performance goal for 510(k) submissions for combination products and companion diagnostic devices that involve consultations outside the Center. Industry requested data on CDRH review times as well as the review times from other Centers providing consulting reviews. FDA explained that such data are not available, given the current internal tracking systems. FDA noted that CDRH often must address complex regulatory issues within the review of a combination product submission. As FDA is being asked to improve 510(k) performance in MDUFA III, this separate goal will mitigate the unintended consequence of negative decisions when there is not sufficient time to work through outstanding drug issues. Industry asked the approximate size of the cohort; the Agency estimated 300-400 per year. Industry stated that if a separate goal is to be considered, historical 510(k) performance data should be re-presented with these submissions separated out. Industry also noted the statutory requirement for the Office of Combination Products to “ensure timely and effective premarket reviews by overseeing the timeliness of and coordinating reviews involving more than one agency center.”

FDA noted that they do not currently have the resources to reduce the ratio of review staff to front-line supervisors without moving internal review staff into management positions in the Pre-Market review program. Shifting resources in this way will have the positive impact on improving consistency and predictability, but will negatively impact performance since there will be less staff doing reviews. Industry stated their displeasure in what was perceived as FDA’s assumption that Industry would pay for the publicly announced reorganization plan. FDA clarified that a reorganization of CDRH has been proposed publicly as a potential means of addressing concerns regarding consistency, predictability, and transparency. FDA has not committed to moving forward with this proposal due to the current lack of resources to implement the plan, but acknowledged that the current organizational structure needs to change in order to effectively carry out its public health mission.

FDA also noted that the Reviewer Certification Program is planned for internal CDRH reviewers only; Third Party reviewers will continue to be trained separately.

FDA followed up on past discussions by providing Industry a list of objective criteria for RTA and RTF checklists that FDA intends to implement via guidance. The criteria would feature several topics. Administrative items would be: checklist completed by sponsor with page number references, qualification of bundled submissions per guidance, identification of all related submissions with responses to all previous

feedback, and inclusion of an e-copy. Items relating to organization, format, and content would be: grammatically correct English language, labeled sections, numbered pages, and inclusion of a table of contents. Items relating to the device description would be: recommendations from device-specific guidance, principle of operation and mechanism of action for achieving the intended therapeutic/diagnostic effect, conditions of use, user interface, list and description of each model under review, manufacturing process (when applicable), engineering drawings/schematics/illustrations/figures, and information regarding accessories (when applicable). Items relating to the substantial equivalence discussion would be: predicate(s) 510(k) number, trade name, model number, and that the predicate(s) should be consistent throughout the submission. Items relating to biocompatibility would be: list of patient contacting components and materials; identification of contact classification (i.e., duration of patient contact); complete testing of patient contacting components per recognized standards, documented with protocols, methods, pass/fail criteria, results, and rationales for any deviations from standards or a rationale explaining why biocompatibility testing is not necessary. All appropriate elements of guidance documents on patient labeling, sterilization, and software would be included. Items relating to electromagnetic compatibility (EMC) and safety would include: evaluation per IEC 60601-1, IEC 60601-2, device-specific FDA recognized standards, or alternative evaluations with accompanying rationale. Items relating to performance data would include: full test reports for each test (including objective of test, description of test methods and procedures, study endpoint, pre-defined pass/fail criteria, results summary, discussion of conclusions), performance data outlined in device-specific guidance or rationale for omission, identification of any devices used in comparative evaluations as predicates, summary of each test article, device hazard analysis (including description and severity of hazard, cause of hazard, method of hazard control or mitigation, description of testing completed to verify control action adequately mitigates hazard. Items relating to performance data for in vitro diagnostics would also include analytical studies (performance characteristics) and associated protocols, including line data and the following information as applicable: precision (reproducibility at three sites), linearity, detection limits, analytical specificity, assay cut-off, method or clinical outcome comparison, matrix comparison, reference range, disinfection, stability protocol and acceptance criteria.

FDA agreed to apply user fee revenues to supplement the guidance document development process, but noted their intention to prioritize review of premarket submissions if resources are insufficient for both. Industry concurred with the Agency’s prioritization approach. Industry requested a mechanism for timely feedback on guidance documents they draft and submit to FDA for consideration. FDA noted that the existing good guidance practices regulations provide a process for submission of draft guidance documents for the Agency to consider, and FDA indicated it would consider this request.

Regarding interactive review (IR), Industry proposed that reviewers share issues with applicants prior to incorporating them into a formal letter. FDA indicated that it is not always efficient to communicate issues prior to sending a letter, as major issues require supervisory review prior to any communication with the sponsor. Use of IR for these issues prior to sending a letter would require supervisory review of

the same issues twice. FDA also noted that this proposal would be inconsistent with the current guidance document “Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements.” FDA suggested that they continue to follow the existing guidance.

FDA and Industry discussed options for the frequency of reporting various performance measures, and whether they would be reported at the Division level or in aggregate.

Shared Outcome Goals

FDA proposed that a Total Time goal no longer be considered for 180 Day PMA Supplements. Instead, FDA believes it is better to retain the ability to send a Major Deficiency Letter to provide the Agency with more flexibility to obtain information necessary to support a positive decision, even though that flexibility increases total time to a decision for this submission type.

FDA proposed several refinements to the shared outcome goals for average total time to decision. There was discussion regarding the total time goal metrics, how they would be calculated, and when success or failure under the goals could be ascertained, given the need to wait for decisions on a given submission cohort of applications.

For reporting of 510(k) and PMA performance for average Total Time to Decision, FDA incorporated Industry’s proposal for considering cohorts closed when a given percentage of the applications have reached a MDUFA decision in order to make complete cohort data available sooner for timely program analyses. FDA also proposed using a trimmed mean for calculating 510(k) performance and a trimmed mean of the three-year rolling average for calculating PMA performance. Industry agreed to the concepts proposed but noted additional discussion may be necessary regarding the percentages required to consider a cohort closed and the percentages used for trimming of the means.

Next Steps

Both FDA and Industry acknowledged that the robust exchange of different ideas during the meeting and over the past several weeks has accelerated progress toward resolving differences in the qualitative and quantitative performance goal areas. FDA and Industry agreed to continue to work toward resolving these differences in the next several days so that financial resources can be discussed at the next meeting.

Next Meeting

The next meeting will take place October 26, 2011.

Meeting End Time: 5:00 pm

[1] For purposes of these minutes only, the term Industry refers to AdvaMed, MITA,

and MDMA and does not include ACLA unless specifically noted.

SOURCE [2]

Source URL (retrieved on *10/23/2014 - 2:41am*):
http://www.mdtmag.com/news/2011/11/minutes-negotiation-meeting-mdufa-iii-reauthorization-october-21-2011

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