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MDUFA Performance Goals and Procedures

The performance goals and procedures agreed to by the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (“FDA” or “the Agency”) for the medical device user fee program in the Medical Device User Fee Amendments of 2012, are summarized below.

FDA and the industry are committed to protecting and promoting public health by providing timely access to safe and effective medical devices. Nothing in this letter precludes the Agency from protecting the public health by exercising its authority to provide a reasonable assurance of the safety and effectiveness of medical devices. Both FDA and the industry are committed to the spirit and intent of the goals described in this letter.

I. Process Improvements

A. Pre-Submissions

FDA will institute a structured process for managing Pre-Submissions. Pre-Submissions subject to this process are defined in Section VIII, Definitions and Explanations of Terms. The Agency will continue to improve the Pre-Submission process as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations. FDA will issue a draft guidance document and final guidance document on Pre-Submissions.

Upon receipt of a Pre-Submission that requests feedback through a meeting or teleconference, FDA intends to schedule the meeting or teleconference to occur within a timely manner. In the Pre-Submission, the applicant will provide at least three suggested dates and times when the applicant is available to meet.

It is FDA’s intent that within 14 calendar days of receipt of a request for a meeting or teleconference, FDA will determine if the request meets the definition of a Pre-Submission, and will inform the applicant if it does not meet the definition. FDA will also determine if the request necessitates more than one meeting or teleconference. A determination that the request does not meet the definition of a Pre-Submission will require the concurrence of the branch chief and the reason for this determination will be provided to the applicant. If the request meets the definition of a Pre-Submission, FDA and the applicant will set a mutually agreeable time and date for the meeting.

At least 3 business days prior to the meeting, FDA will provide initial feedback to the applicant by email, which will include: written responses to the applicant’s questions; FDA’s suggestions for additional topics for the meeting or teleconference, if applicable; or, a combination of both. If all of the applicant’s questions are addressed through written responses, to the applicant’s satisfaction, FDA and the applicant can agree that a meeting

or teleconference is no longer necessary and the written responses provided by email will be considered the final written feedback to the Pre-Submission.

Meetings and teleconferences related to Pre-Submission will generally be limited to 1 hour. A longer meeting or teleconference time can be scheduled by mutual agreement by the applicant and FDA.

Applicants will be responsible for developing draft minutes for a Pre-Submission meeting or teleconference, and provide the draft minutes via email to FDA within 15 calendar days of the meeting. The minutes will summarize the meeting discussions and include agreements and any action items. FDA will provide any edits to the draft minutes to the applicant via email within a timely manner. These minutes will become final 15 calendar days after the applicant receives FDA's edits, unless the applicant indicates that there is a disagreement with how a significant issue or action item has been documented. In this case, within a timely manner, the applicant and FDA will conduct a teleconference to discuss that issue with FDA. At the conclusion of that teleconference, within a timely manner FDA will finalize the minutes either to reflect the resolution of the issue or note that this issue remains a point of disagreement.

FDA intends that feedback the Agency provides in a Pre-Submission will not change, provided that the information submitted in a future investigational device exemption (IDE) or marketing application is consistent with that provided in the Pre-Submission and that the data in the future submission do not raise any important new issues materially affecting safety or effectiveness. Modifications to FDA's feedback will be limited to situations in which FDA concludes that the feedback does not adequately address important new issues materially relevant to a determination of safety or effectiveness. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs.

B. Submission Acceptance Criteria

To facilitate a more efficient and timely review process, FDA will implement revised submission acceptance criteria. The Agency will publish guidance outlining electronic copy of submissions (e-Copy) and objective criteria for revised "refuse to accept/refuse to file" checklists. FDA will publish draft and final guidance prior to implementation.

C. Interactive Review

The Agency will continue to incorporate an interactive review process to provide for, and encourage, informal communication between FDA and applicants to facilitate timely completion of the review process based on accurate and complete information.

Interactive review entails responsibilities for both FDA and applicants. As described in the guidance document, *Interactive Review for Medical Device Submissions: 510(k)s, Original [Premarket Approvals] PMAs, PMA Supplements, Original BLAs, and BLA Supplements*, both FDA and industry believe that an interactive review process for these types of premarket medical device submissions should help facilitate timely completion of the review based on accurate and complete information. Interactive review is intended to facilitate the efficient and timely review and evaluation by FDA of premarket submissions. The interactive review process contemplates increased informal interaction between FDA and applicants, including the exchange of scientific and regulatory information.

D. Guidance Document Development

FDA will apply user fee revenues to supplement the improvement of the process of developing, reviewing, tracking, issuing, and updating guidance documents. The Agency will continue to develop guidance documents and improve the Guidance Development process as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations.

FDA will update its website in a timely manner to reflect the following:

1. The Agency's review of previously published device guidance documents, including the deletion of guidance documents that no longer represent the Agency's interpretation of, or policy on, a regulatory issue, and notation of guidance documents that are under review by the Agency;
2. A list of prioritized device guidance documents (an "A-list") that the Agency intends to publish within 12 months of the date this list is published each fiscal year; and
3. A list of device guidance documents (a "B-list") that the Agency intends to publish, as the Agency's guidance-development resources permit each fiscal year.

The Agency will establish a process allowing stakeholders an opportunity to:

1. Provide meaningful comments and/or propose draft language for proposed guidance topics in the "A" and "B" lists.
2. Provide suggestions for new or different guidance documents; and
3. Comment on the relative priority of topics for guidance.

E. Third Party Review

The Agency will continue to support the third party review program and agrees to work with interested parties to strengthen and improve the current program while also establishing new procedures to improve transparency. The Agency will continue to

improve the third party review program as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations.

F. Patient Safety and Risk Tolerance

FDA will fully implement final guidance on the factors to consider when making benefit-risk determinations in medical device premarket review. This guidance will focus on factors to consider in the premarket review process, including patient tolerance for risk, magnitude of the benefit, and the availability of other treatments or diagnostic tests.

Over the period of MDUFA III, FDA will meet with patient groups to better understand and characterize the patient perspective on disease severity or unmet medical need.

In addition, FDA will increase its utilization of FDA's Patient Representatives as Special Government Employee consultants to CDRH to provide patients' views early in the medical product development process and ensure those perspectives are considered in regulatory discussions. Applicable procedures governing conflicts of interest and confidentiality of proprietary information will be utilized for these consultations.

G. Low Risk Medical Device Exemptions

By the end of FY 2013, FDA will propose additional low risk medical devices to exempt from premarket notification. Within two years of such proposal, FDA intends to issue a final rule exempting additional low risk medical devices from premarket notification.

H. Emerging Diagnostics

FDA will work with industry to develop a transitional In Vitro Diagnostics (IVD) approach for the regulation of emerging diagnostics.

II. Review Performance Goals - Fiscal Years 2013 Through 2017 As Applied to Receipt Cohorts

The overall objective of the review performance goals stated herein is to assure more timely access to safe and effective medical devices.

A. Original Premarket Approval (PMA), Panel-Track Supplements, and Premarket Report Applications

The performance goals in this section apply to all Original Premarket Approval, Panel-Track Supplements, and Premarket Report Applications, including those that are accepted for priority review (previously referred to as expedited).

FDA will communicate with the applicant regarding whether the application has been accepted for filing review within 15 calendar days of receipt of the application. This

communication consists of a fax, email, or other written communication that a) identifies the reviewer assigned to the submission, and b) acknowledges acceptance/rejection of the submission based upon the review of the submission against objective acceptance criteria outlined in a published guidance document.

If the application is not accepted for filing review, FDA will notify the applicant of those items necessary for the application to be considered accepted for filing review.

For those applications that are accepted for filing review, FDA will communicate the filing status within 45 calendar days of receipt of the application.

For those applications that are not filed, FDA will communicate to the applicant the specific reasons for rejection and the information necessary for filing.

If the application is filed, FDA will communicate with the applicant through a Substantive Interaction within 90 calendar days of the filing date of the application for: 65% of submissions received in FY 2013; 75% of submissions received in FY 2014; 85% of submissions received in FY 2015; and 95% of submissions received in FY 2016 through FY 2017.

When FDA issues a major deficiency letter, that letter will be based upon a complete review of the application and will include all deficiencies. Any subsequent deficiencies will be limited to issues raised by the information provided by the applicant in its response, unless FDA concludes that the initial deficiencies identified do not adequately address important new issues materially relevant to a determination of safety or effectiveness. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs. Issues related to post-approval studies, if applicable, and revisions to draft labeling will typically be addressed through interactive review once major deficiencies have been adequately addressed.

For submissions that do not require Advisory Committee input, FDA will issue a MDUFA decision within 180 FDA Days for: 70% of submissions received in FY 2013; 80% of submissions received in FY 2014 and FY 2015; and 90% of submissions received in FY 2016 and FY 2017.

For submissions that require Advisory Committee input, FDA will issue a MDUFA decision within 320 FDA Days for: 50% of submissions received in FY 2013; 70% of submissions received in FY 2014; 80% of submissions received in FY 2015 and FY 2016; and 90% of submissions received in FY 2017.

If in any one fiscal year, the number of submissions that require Advisory Committee input is less than 10, then it is acceptable to combine such submissions with the submissions for the following year(s) in order to form a cohort of 10 or more submissions, upon which the combined years' submissions will be subject to the performance goal for the fiscal year in question. If the number of submissions that require Advisory Committee input is less than 10 for FY 2017, it is acceptable to

combine such submissions with the submissions in the prior year in order to form a cohort of 10 or more submissions; in such cases, FDA will be held to the FY 2017 performance goal for the combined years' submissions.

To facilitate an efficient review prior to the Substantive Interaction, and to incentivize submission of a complete application, submission of an unsolicited major amendment prior to the Substantive Interaction extends the FDA Day review clock by the number of FDA Days that have elapsed. Submission of an unsolicited major amendment after the Substantive Interaction extends the FDA Day goal by the number of FDA Days equal to 75% of the difference between the filing date and the date of receipt of the amendment.

For all PMA submissions that do not reach a MDUFA decision by 20 days after the applicable FDA Day goal, FDA will provide written feedback to the applicant to be discussed in a meeting or teleconference, including all outstanding issues with the application preventing FDA from reaching a decision. The information provided will reflect appropriate management input and approval, and will include action items for FDA and/or the applicant, as appropriate, with an estimated date of completion for each party to complete their respective tasks. Issues should be resolved through interactive review. If all of the outstanding issues are adequately presented through written correspondence, FDA and the applicant can agree that a meeting or teleconference is not necessary.

In addition, information about submissions that miss the FDA Day goal will be provided as part of FDA's Performance Reports, as described in Section VI.

B. 180-Day PMA Supplements

FDA will communicate with the applicant through a Substantive Interaction within 90 calendar days of receipt of the submission for: 65% of submissions received in FY 2013; 75% of submissions received in FY 2014; 85% of submissions received in FY 2015; and 95% of submissions received in FY 2016 through FY 2017.

FDA will issue a MDUFA decision within 180 FDA Days for: 85% of submissions received in FY 2013; 90% of submissions received in FY 2014 and FY 2015; and 95% of submissions received in FY 2016 through FY 2017.

C. Real-Time PMA Supplements

FDA will issue a MDUFA decision within 90 FDA Days for: 90% of submissions received in FY 2013 and FY 2014; and 95% of submissions received in FY 2015 through FY 2017.

D. 510(k) Submissions

FDA will communicate with the applicant regarding whether the submission has been accepted for review within 15 calendar days of receipt of the submission. For those submissions that are not accepted for review, FDA will notify the applicant of those items necessary for the submission to be considered accepted.

This communication includes a fax, email, or other written communication that a) identifies the reviewer assigned to the submission, and b) acknowledges acceptance/rejection of the submission based upon the review of the submission against objective acceptance criteria outlined in a published guidance document. This communication represents a preliminary review of the submission and is not indicative of deficiencies that may be identified later in the review cycle.

FDA will communicate with the applicant through a Substantive Interaction within 60 calendar days of receipt of the submission for: 65% of submissions received in FY 2013; 75% of submissions received in FY 2014; 85% of submissions received in FY 2015; and 95% of submissions received in FY 2016 through FY 2017.

Deficiencies identified in a Substantive Interaction, such as a telephone/email hold or Additional Information Letter, will be based upon a complete review of the submission and will include all deficiencies. Any subsequent deficiencies will be limited to issues raised by the information provided by the applicant in its response, unless FDA concludes that the initial deficiencies identified do not adequately address important new issues materially relevant to a determination of substantial equivalence. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs.

For submissions received in FY 2013, FDA will issue a MDUFA decision for 91% of 510(k) submissions within 90 FDA Days.

For submissions received in FY 2014, FDA will issue a MDUFA decision for 93% of 510(k) submissions within 90 FDA Days.

For submissions received in FY 2015 through FY 2017, FDA will issue a MDUFA decision for 95% of 510(k) submissions within 90 FDA Days.

For all 510(k) submissions that do not reach a MDUFA decision within 100 FDA Days, FDA will provide written feedback to the applicant to be discussed in a meeting or teleconference, including all outstanding issues with the application preventing FDA from reaching a decision. The information provided will reflect appropriate management input and approval, and will include action items for FDA and/or the applicant, as appropriate, with an estimated date of completion for each party to complete their respective tasks. Issues should be resolved through interactive review. If all of the outstanding issues are adequately presented through written correspondence, FDA and the applicant can agree that a meeting or teleconference is not necessary.

In addition, information about submissions that miss the FDA Day goal will be provided as part of FDA's Performance Reports, as described in Section VI.

E. Clinical Laboratory Improvement Amendments (CLIA) Waiver by Application

FDA will engage in a Substantive Interaction with the applicant within 90 days for 95% of the applications.

During the pre-submission process, if the applicant informs FDA that it plans to submit a dual submission (510(k) and CLIA Waiver application), FDA will issue a decision for 90% of such applications within 210 FDA days.

For "CLIA Waiver by application" submissions FDA will issue a MDUFA decision for 95% of the applications that do not require Advisory Committee input within 180 FDA days.

For "CLIA Waiver by application" submissions FDA will issue a MDUFA decision for 95% of the applications that require Advisory Committee input within 330 FDA days.

To provide greater transparency, FDA will issue guidance regarding review and management expectations throughout the entire submission process.

F. Original Biologics Licensing Applications (BLAs)

FDA will review and act on standard original BLA submissions within 10 months of receipt for 90% of submissions.

FDA will review and act on priority original BLA submissions within 6 months of receipt for 90% of submissions.

G. BLA Efficacy Supplements

FDA will review and act on standard BLA efficacy supplement submissions within 10 months of receipt for 90% of submissions.

FDA will review and act on priority BLA efficacy supplement submissions within 6 months of receipt for 90% of submissions.

H. Original BLA and BLA Efficacy Supplement Resubmissions

FDA will review and act on Class 1 original BLA and BLA efficacy supplement resubmissions within 2 months of receipt for 90% of submissions.

FDA will review and act on Class 2 original BLA and BLA efficacy supplement resubmissions within 6 months of receipt for 90% of submissions.

I. BLA Manufacturing Supplements Requiring Prior Approval

FDA will review and act on BLA manufacturing supplements requiring prior approval within 4 months of receipt for 90% of submissions.

III. Shared Outcome Goals

The program and initiatives outlined in this document are predicated on significant interaction between the Agency and applicants. FDA and representatives of the medical device industry agree that the process improvements outlined in this letter, when implemented by all parties as intended, should reduce the average Total Time to Decision for PMA applications and 510(k) submissions, provided that the total funding of the device review program adheres to the assumptions underlying this agreement. FDA and applicants share the responsibility for achieving this objective of reducing the average Total Time to Decision, while maintaining standards for safety and effectiveness. Success of this program will require the cooperation and dedicated efforts of FDA and applicants to reduce their respective portions of the total time to decision.

FDA will be reporting total time performance quarterly as described in Section VI. FDA and industry will participate in the independent assessment of progress toward this outcome, as described in Section V above. As appropriate, key findings and recommendations from this assessment will be implemented by FDA.

A. PMA

Beginning in Fiscal Year 2013, FDA will report on an annual basis the average Total Time to Decision as defined in Section VIII.G for the three most recent closed receipt cohorts. For submissions received beginning in Fiscal Year 2013, the average Total Time to Decision goal for FDA and industry is 395 calendar days. For submissions received beginning in Fiscal Year 2015, the average Total Time to Decision goal for FDA and industry is 390 calendar days. For submissions received beginning in Fiscal Year 2017, the average Total Time to Decision goal for FDA and industry is 385 calendar days.

B. 510(k)

Beginning in Fiscal Year 2013, FDA will report on an annual basis the average Total Time to Decision as defined in Section VIII.G for the most recent closed receipt cohort. For submissions received beginning in Fiscal Year 2013, the average Total Time to Decision goal for FDA and industry is 135 calendar days. For submissions received beginning in FY 2015, the average Total Time to Decision goal for FDA and industry is 130 calendar days. For submissions received beginning in FY 2017, the average Total Time to Decision goal for FDA and industry is 124 calendar days.

IV. Infrastructure

A. Scientific and Regulatory Review Capacity

The Agency will apply user fee revenues to reduce the ratio of review staff to front line supervisors in the Pre-Market review program and to enhance and supplement scientific review capacity by hiring device application reviewers and leveraging external experts needed to assist with the review of device applications.

The Agency will seek to obtain streamlined hiring authority for all MDUFA-related positions prior to and during the MDUFA III period.

During MDUFA III, FDA will also work with industry to benchmark best practices for retaining employees (both financial and non-financial).

B. Training

Prior to the commencement of MDUFA III, CDRH will implement its Reviewer Certification Program. FDA commits to holding a minimum of two medical device Vendor Days each year.

CDRH will apply user fee revenues to supplement the following training programs:

- 1) Management training for Branch Chiefs and Division Directors.
- 2) MDUFA III Training Program for all staff.
- 3) Reviewer Certification Program for new CDRH reviewers. FDA will publish the curriculum of this program and other course offerings. FDA will consider comments from stakeholders when making updates to courses and determining course offerings.
- 4) Specialized training to provide continuous learning for all staff.

C. Tracking System

FDA will continue efforts to improve its IT systems with a future expectation of facilitating availability of real-time status information for submissions.

V. Independent Assessment of Review Process Management

FDA and the device industry will participate in a comprehensive assessment of the process for the review of device applications. The assessment will include consultation with both FDA and industry. The assessment shall be conducted in two phases under contract to FDA by a private, independent consulting firm capable of performing the technical analysis, management assessment, and program evaluation tasks required to address the assessment scope described below. For Phase 1, FDA will award the

contract no later than the end of the second quarter of FY13. Findings on high-priority recommendations (i.e., those likely to have a significant impact on review times) will be published within six months of award; final comprehensive findings and recommendations will be published within 1 year of contract award. FDA will publish an implementation plan within 6 months of receipt of each set of recommendations. For Phase 2 of the independent assessment, the contractor will evaluate the implementation of recommendations and publish a written assessment no later than February 1, 2016.

The assessment will address FDA's premarket review process using an assessment framework that draws from appropriate quality system standards, including, but not limited to, management responsibility, document controls and records management, and corrective and preventive action.

The scope of the assessment will include, but not be limited to, the following areas:

1. Identification of process improvements and best practices for conducting predictable, efficient, and consistent premarket reviews that meet regulatory review standards.
2. Analysis of elements of the review process (including the Pre-Submission process, IDE, 510(k) and PMA reviews) that consume or save time to facilitate a more efficient process. This includes analysis of root causes for inefficiencies that may affect review performance and total time to decision. This will also include recommended actions to correct any failures to meet MDUFA goals. Analysis of the review process will include the impact of combination products, companion diagnostics products, and laboratory developed tests on the review process.
3. Assessment of FDA methods and controls for collecting and reporting information on premarket review process resource use and performance.
4. Assessment of effectiveness of FDA's Reviewer Training Program implementation.
5. Recommendations for ongoing periodic assessments and any additional, more detailed or focused assessments.

FDA will incorporate findings and recommendations, as appropriate, into its management of the premarket review program. FDA will analyze the recommendations for improvement opportunities identified in the assessment, develop and implement a corrective action plan, and assure its effectiveness. FDA also will incorporate the results of the assessment into a Good Review Management Practices (GRMP) guidance document. FDA's implementation of the GRMP guidance will include initial and ongoing training of FDA staff, and periodic audits of compliance with the guidance.

VI. Performance Reports

The Agency will report its progress toward meeting the goals described in this letter, as follows. If, throughout the course of MDUFA III, the Agency and Industry agree that a

different format or different metrics would be more useful, the reporting will be modified accordingly as per the agreement of both FDA and Industry.

1. Quarterly reporting at the CDRH Division level/CBER Center level (in recognition of the significantly smaller number of submissions reviewed at CBER):
 - 1.1. For 510(k) submissions, reporting will include:
 - i. Average and quintiles of the number of calendar days to Substantive Interaction
 - ii. Average, and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision
 - iii. Average number of review cycles.
 - iv. Rate of submissions not accepted for review
 - 1.2. For PMA submissions, reporting will include:
 - i. Average and quintiles of the number of calendar days to Substantive Interaction for Original PMA, Panel-Track PMA Supplement, and Premarket Report Submissions
 - ii. Average and quintiles of the of FDA Days, Industry Days, and Total Days to a MDUFA decision
 - iii. Rate of applications not accepted for filing review, and rate of applications not filed
 - 1.3. For Pre-Submissions, reporting will include:
 - i. Number of all qualified Pre-Submissions received
 - ii. Average and quintiles of the number of calendar days from submission to meeting or teleconference (if necessary)
 - iii. Number of Pre-Submissions that require a meeting
 - 1.4. For IDE applications, reporting will include:
 - i. Number of original IDEs received
 - ii. Average number of amendments prior to approval or conditional approval of the IDE (this information will be provided beginning no later than the quarter that starts 10/1/2013)
2. CDRH will report quarterly, and CBER will report annually, the following data at the Center level:
 - 2.1. Rate of NSE decisions for 510(k) submissions
 - 2.2. Rate of withdrawals for 510(k) and PMA submissions
 - 2.3. Rate of Not Approvable decisions for PMA submissions
 - 2.4. Key product areas or other issues that FDA identifies as noteworthy because of a potential effect on performance, including significant rates of Additional Information requests
 - 2.5. Specific topic or product area as it relates to performance goals, agreed upon at the previous meeting
 - 2.6. Number of submissions that missed the goals and the total number of elapsed calendar days broken down into FDA days and industry days
 - 2.7. Newly released draft and final guidance documents, and status of other priority guidance documents
 - 2.8. Agency level summary of fee collections

- 2.9. Independent assessment implementation plan status
 - 2.10. Results of independent assessment and subsequent periodic audits and progress toward implementation of the recommendations and any corrective action
 - 2.11. Number of discretionary fee waivers or reductions granted by type of submission
3. In addition, the Agency will provide the following information on an annual basis:
- 3.1. Qualitative and quantitative update on how funding is being used for the device review process, including the percentage of review time devoted to direct review of applications
 - 3.2. How funding is being used to enhance scientific review capacity
 - 3.3. The number of Premarket Report Submissions received
 - 3.4. Summary information on training courses available to CDRH and CBER employees, including new reviewers, regarding device review and the percentage of applicable staff that have successfully completed each such course. CDRH will provide information concerning any revisions to the new reviewer training program curriculum.
 - 3.5. Performance on the shared outcome goal for average Total Time to decision
 - 3.6. For 510(k) submissions, reporting will include:
 - i. Number of submissions reviewed by a Third Party
 - ii. Number of Special Submissions
 - iii. Number of Traditional Submissions
 - iv. Average and number of days to Accept/Refuse to Accept
 - v. Number of Abbreviated Submissions
 - 3.7. For PMA submissions, reporting will include the number of the following types of PMA submissions received:
 - i. Original PMAs
 - ii. Priority PMAs
 - iii. Premarket Reports
 - iv. Panel-Track PMA Supplement
 - v. PMA Modules
 - vi. 180-Day PMA Supplements
 - vii. Real-Time PMA Supplements
 - 3.8. For De Novo Classification Petitions, reporting will include:
 - i. Number of submissions received
 - ii. Average number of calendar days to a MDUFA decision
 - 3.9. For CLIA waiver applications, reporting will include:
 - i. Number of CLIA waiver applications received
 - ii. Average and quintiles of the number of calendar days to Substantive Interaction
 - iii. Average and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision and a discussion of any trends in the data

VII. Discretionary Waiver

The Agency will seek authority to grant discretionary fee waivers or reductions in the interest of public health. Notwithstanding any fee waivers or reductions granted by the Agency under this discretionary authority, FDA remains committed to meeting the goals described in this letter. Any submission subject to a fee waiver or reduction under this discretionary authority shall not be subject to the goals specified in this letter and shall be reviewed by the Agency as resources permit. This discretionary authority will expire at the end of MDUFA III.

VIII. Definitions and Explanations of Terms

A. Applicant

Applicant means a person who makes any of the following submissions to FDA:

- an application for premarket approval under section 515;
- a premarket notification under section 510(k);
- an application for investigational device exemption under section 520(g);
- a Pre-Submission;
- a CLIA waiver application.

B. Electronic Copy (e-Copy)

An electronic copy is an exact duplicate of a paper submission, created and submitted on a CD, DVD, or in another electronic media format that FDA has agreed to accept, accompanied by a copy of the signed cover letter and the complete original paper submission. An electronic copy is not considered to be an electronic submission.

C. FDA Days

FDA Days are those calendar days when a submission is considered to be under review at the Agency for submissions that have been accepted (510(k)) or filed (PMA). FDA Days begin on the date of receipt of the submission or of the amendment to the submission that enables the submission to be accepted (510(k)) or filed (PMA).

D. MDUFA Decisions

Original PMAs: Decisions for Original PMAs are Approval, Approvable, Approvable Pending GMP Inspection, Not Approvable, Withdrawal, and Denial.

180-Day PMA Supplements: Decisions for 180-Day PMA Supplements include Approval, Approvable, and Not Approvable.

Real-Time PMA Supplements: Decisions for Real-Time PMA supplements include Approval, Approvable, and not Approvable.

510(k)s: Decisions for 510(k)s are substantially equivalent (SE) or not substantially equivalent (NSE).

Submissions placed on Application Integrity Program Hold will be removed from the MDUFA cohort.

E. Pre-Submission

A Pre-Submission includes a formal written request from an applicant for feedback from FDA which is provided in the form of a formal written response or, if the manufacturer chooses, a meeting or teleconference in which the feedback is documented in meeting minutes. A Pre-Submission meeting is a meeting or teleconference in which FDA provides its substantive feedback on the Pre-Submission.

A Pre-Submission provides the opportunity for an applicant to obtain FDA feedback prior to intended submission of an investigational device exemption or marketing application. The request must include specific questions regarding review issues relevant to a planned IDE or marketing application (e.g., questions regarding pre-clinical and clinical testing protocols or data requirements). A Pre-Submission is appropriate when FDA's feedback on specific questions is necessary to guide product development and/or application preparation.

The following forms of FDA feedback to applicants are not considered Pre-Submissions. However, if the requested feedback meets the criteria for a Pre-Submission, outlined above, FDA will contact the sponsor, and with the concurrence of the sponsor, may convert the request to a Pre-Submission.

- General information requests initiated through the Division of Small Manufacturers, International and Consumer Assistance (DSMICA)
- General questions regarding FDA policy or procedures
- Meetings or teleconferences that are intended to be informational only, including, but not limited to, those intended to educate the review team on new device(s) with significant differences in technology from currently available devices, or to update FDA about ongoing or future product development, without a request for FDA feedback on specific questions related to a planned submission
- Requests for clarification on technical guidance documents, especially where contact is recommended by FDA in the guidance document. However, the following requests will generally need to be submitted as a Pre-Submission in order to ensure appropriate input from multiple reviewers and management:

recommendations for device types not specifically addressed in the guidance document; recommendations for nonclinical or clinical studies not addressed in the guidance document; requests to use an alternative means to address recommendations specified in a guidance document.

- Phone calls or email messages to reviewers that can be readily answered based on a reviewer's experience and knowledge and do not require the involvement of a broader number of FDA staff beyond the routine involvement of the reviewer's supervisor and more experienced mentors.
- Interactions requested by either the applicant or FDA during the review of a marketing application (i.e., following submission of a marketing application, but prior to reaching an FDA Decision).

F. Substantive Interaction

Substantive Interaction is an email, letter, teleconference, video conference, fax, or other form of communication such as a request for Additional Information or Major Deficiency letters by FDA notifying the applicant of substantive deficiencies identified in initial submission review, or a communication stating that FDA has not identified any deficiencies in the initial submission review and any further minor deficiencies will be communicated through interactive review. An approval or clearance letter issued prior to the Substantive Interaction goal date will qualify as a Substantive Interaction.

If substantive issues warranting issuance of an Additional Information or Major Deficiency letter are not identified, interactive review should be used to resolve any minor issues and facilitate an FDA decision. In addition, interactive review will be used, where, in FDA's estimation, it leads to a more efficient review process during the initial review cycle (i.e., prior to a Substantive Interaction) to resolve minor issues such as revisions to administrative items (e.g., 510(k) Summary/Statement, Indications for Use statement, environmental impact assessment, financial disclosure statements); a more detailed device description; omitted engineering drawings; revisions to labeling; or clarification regarding nonclinical or clinical study methods or data.

Minor issues may still be included in an Additional Information or Major Deficiency letter where related to the resolution of the substantive issues (e.g., modification of the proposed Indications for Use may lead to revisions in labeling and administrative items), or if they were still unresolved following interactive review attempts. Both interactive review and Substantive Interactions will occur on the review clock except upon the issuance of an Additional Information or Major Deficiency Letter which stops the review clock.

G. Total Time to Decision

Total Time to Decision is the number of calendar days from the date of receipt of an accepted or filed submission to a MDUFA decision.

The average Total Time to Decision for 510(k) submissions is calculated as the trimmed mean of Total Times to Decision for 510(k) submissions within a closed cohort, excluding the highest 2% and the lowest 2% of values. A cohort is closed when 99% of the accepted submissions have reached a decision.

The average Total Time to Decision for PMA applications is calculated as the three-year rolling average of the annual Total Times to Decision for applications (for example, for FY2015, the average Total Time to Decision for PMA applications would be the average of FY2013 through FY2015) within a closed cohort, excluding the highest 5% and the lowest 5% of values. A cohort is closed when 95% of the applications have reached a decision.

H. BLA-related Definitions

Review and act on – the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.

Class 1 resubmitted applications – applications resubmitted after a complete response letter that includes the following items only (or combinations of these items):

- (a) Final printed labeling
- (b) Draft labeling
- (c) Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information including important new adverse experiences not previously reported with the product are presented in the resubmission)
- (d) Stability updates to support provisional or final dating periods
- (e) Commitments to perform Phase 4 studies, including proposals for such studies
- (f) Assay validation data
- (g) Final release testing on the last 1-2 lots used to support approval
- (h) A minor reanalysis of data previously submitted to the application (determined by the Agency as fitting the Class 1 category)
- (i) Other minor clarifying information (determined by the Agency as fitting the Class 1 category)
- (j) Other specific items may be added later as the Agency gains experience with the scheme and will be communicated via guidance documents to industry

Class 2 resubmitted applications – resubmissions that include any other items, including any item that would require presentation to an advisory committee

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