MDUFA PERFORMANCE GOALS AND PROCEDURES, FISCAL YEARS 2018 THROUGH 2022

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General

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 2017, 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. 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 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 below. As appropriate, key findings and recommendations from this assessment will be implemented by FDA.

A. PMA

FDA will report on an annual basis the average Total Time to Decision as defined in Section VII.H for the three most recent closed receipt cohorts.

For Original PMA and Panel Track Supplement submissions received in Fiscal Years 2016 through 2018, the average Total Time to Decision goal for FDA and industry is 320 calendar days.

For Original PMA and Panel Track Supplement submissions received in Fiscal Years 2017 through 2019, the average Total Time to Decision goal for FDA and industry is 315 calendar days.

For Original PMA and Panel Track Supplement submissions received in Fiscal Years 2018 through 2020, the average Total Time to Decision goal for FDA and industry is 310 calendar days.

For Original PMA and Panel Track Supplement submissions received in Fiscal Years 2019 through 2021, the average Total Time to Decision goal for FDA and industry is 300 calendar days.

For Original PMA and Panel Track Supplement submissions received in Fiscal Years 2020 through 2022, the average Total Time to Decision goal for FDA and industry is 290 calendar days.

B. 510(k)

FDA will report on an annual basis the average Total Time to Decision as defined in Section VII.H for the most recent closed receipt cohort.

For 510(k) submissions received beginning in Fiscal Year 2018, the average Total Time to Decision goal for FDA and industry is 124 calendar days.

For 510(k) submissions received beginning in Fiscal Year 2019, the average Total Time to Decision goal for FDA and industry is 120 calendar days.

For 510(k) submissions received beginning in Fiscal Year 2020, the average Total Time to Decision goal for FDA and industry is 116 calendar days.

For 510(k) submissions received beginning in Fiscal Year 2021, the average Total Time to Decision goal for FDA and industry is 112 calendar days.

For 510(k) submissions received beginning in Fiscal Year 2022, the average Total Time to Decision goal for FDA and industry is 108 calendar days.

II. Review Performance Goals - Fiscal Years 2018 Through 2022 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. Pre-Submissions

FDA will continue the Pre-Submission program as described in the Guidance on "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff" with process improvements and performance goals as noted in this section.

For all Pre-Submissions in which the applicant requests a meeting or teleconference, the applicant will provide a minimum of three proposed meeting dates in the initial submission.

Within 15 calendar days of receipt of a Pre-Submission, FDA will communicate with the applicant regarding whether the application has been accepted and, if applicable, regarding scheduling of the meeting or teleconference. Acceptance will be determined based on the definition of pre-submission in Section VII.F below and an acceptance checklist in published guidance. This communication consists of a fax, email, or other written communication that a) identifies the reviewer assigned to the submission, b) acknowledges acceptance/rejection of the submission, and c) if the submission included a request for a meeting or teleconference and is accepted, either confirms one of the applicant's requested meeting dates or provides two alternative dates prior to day 75 from receipt of accepted submission. A determination that the request does not qualify as a Pre-Submission will require the concurrence of the branch chief and the reason for this determination will be provided to the applicant in the above written communication. FDA intends to reach agreement with the applicant regarding a meeting date within 30 days from receipt of accepted submission. For all requests for meetings or teleconferences that do not have such a meeting or teleconference scheduled by 30 days from receipt of an accepted submission, an FDA manager will contact the applicant to resolve scheduling issues by the 40th day.

FDA will provide written feedback that addresses the issues raised in the pre-submission request within 70 calendar days of receipt date or five calendar days prior to a scheduled meeting, whichever comes sooner, for at least 1,530 Pre-Submissions received in FY 2018, at least 1,645 Pre-Submissions received in FY 2019, at least 1,765 Pre-Submissions received in FY 2020, at least 1,880 Pre-Submissions received in FY 2021, and at least 1,950 Pre-Submissions received in FY 2022. FDA will provide such timely written feedback for additional Pre-Submissions as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations. Written feedback will be provided to the applicant by email or fax and 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 or fax will be considered the final written feedback to the Pre-Submission.

Meetings and teleconferences related to Pre-Submission will normally be limited to 1 hour unless the applicant justifies in writing the need for additional time. FDA may extend the time for such meetings and/or teleconferences.

Applicants will be responsible for developing draft minutes for a Pre-Submission meeting or teleconference, and provide the draft minutes to FDA within 15 calendar days of the meeting. At the beginning and end of each meeting, the applicant will affirmatively state that they will draft minutes and provide them to FDA within 15 calendar days. 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 15 days 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 the information submitted in a future IDE or marketing application is consistent with that provided in the Pre-Submission and documented in the Pre-Submission, and that the data and other information in the future submission do not raise any important new issues materially affecting safety or effectiveness. The minutes described above will serve as the record of the Agency's Pre-Submission feedback. 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 and/or effectiveness or substantial equivalence. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs.

By October 1, 2018, the Agency will update the Guidance on "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff" to include: additional information to assist applicants in determining the need for a Pre-Submission, an enhanced Pre-Submission acceptance checklist, examples of frequently asked Pre-Submission questions that lend themselves to productive Pre-Submission interactions, and edits to reflect the revised process outlined above. FDA will provide an opportunity for the public to comment on the updated guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement this guidance once final.

B. 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 and consistent with the statute and its implementing regulations.

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 95% of submissions.

When FDA issues a major deficiency letter, that letter will be based upon a complete review of the application and will include all deficiencies. All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a determination of safety and effectiveness. 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 90% of submissions.

For submissions that require Advisory Committee input, FDA will issue a MDUFA decision within 320 FDA Days from receipt of the accepted submission for 90% of submissions. FDA will issue a MDUFA decision within 60 days of the Advisory Committee recommendation, as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations. The Office Director shall review each request for Advisory Committee input for appropriateness and need for this input.

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. If the number of submissions that require Advisory Committee input is less than 10 for FY 2022, it is acceptable to combine such submissions in the prior year to form a cohort of 10 or more submissions: in such cases, FDA will be held to the FY2022 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. Requests from FDA that a submission be made will not be considered unsolicited.

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.

For PMA submissions that receive a MDUFA decision of Approvable, FDA will issue a decision within 60 days of the sponsor's response to the Approvable letter, as resources permit, but not to the detriment of meeting the quantitative review timelines and statutory obligations.

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.

C. 180-Day PMA Supplements

FDA will communicate with the applicant through a Substantive Interaction within 90 calendar days of receipt of 95% of submissions.

FDA will issue a MDUFA decision within 180 FDA Days for 95% of submissions.

D. Real-Time PMA Supplements

FDA will issue a MDUFA decision within 90 FDA Days for 95% of submissions.

E. De Novo Submissions

FDA will issue draft and final guidance that includes a submission checklist to facilitate a more efficient and timely review process.

Deficiencies identified will be based upon a complete review of the submission and will include all deficiencies. All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a classification determination. 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 classification determination. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs. Issues related to revisions to draft labeling will typically be addressed through interactive review once major deficiencies have been adequately addressed.

FDA will issue a MDUFA decision within 150 FDA days of receipt of the submission for: 50% of *de novo* requests received in FY 2018; 55% of *de novo* requests received in FY 2019; 60% of *de novo* requests received in FY 2020; 65% of *de novo* requests received in FY 2021 and 70% of *de novo* requests received in FY 2022. At Industry's request and as resources permit, but not to the detriment of meeting the quantitative review timelines, if a final decision has not been rendered within 180 FDA days, FDA will discuss with the applicant all outstanding issues with the submission preventing FDA from reaching a decision. This discussion 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.

F. 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 95% of submissions.

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. All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a determination of substantial equivalence. 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.

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.

G. CLIA Waiver by Application

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

Industry will inform FDA that it plans to submit a dual submission (510(k) and CLIA Waiver application) during the Pre-Submission process. FDA will issue a decision for 90% of dual submission applications within 180 FDA days.

For "CLIA Waiver by application" submissions FDA will issue a MDUFA decision for 90% of the applications that do not require Advisory Committee input within 150 FDA days.

For "CLIA Waiver by application" submissions FDA will issue a MDUFA decision for 90% of the applications that require Advisory Committee input within 320 FDA days.

If in any one fiscal year, the number of submissions in any CLIA Waiver by Application category 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 all CLIA waiver by application submissions and dual submissions that do not reach a 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.

In addition, FDA will:

1. Hold CLIA Waiver Vendor Days, with the first to occur before the end of FY2018.

2. Permit discussion of both 510(k) and CLIA waiver process in Pre-Submissions.
3. Specifically permit discussion of appropriate reference/comparator for both 510(k) and CLIA waiver submissions in Pre-Submissions.
4. Provide a status report on completion and issuance of revisions to Section V of the Guidance on "Recommendations for CLIA Waiver Applications" to include appropriate use of comparable performance between a waived user and moderately complex laboratory user to demonstrate accuracy.

H. 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.

I. 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.

J. 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.

K. 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. Infrastructure

A. Quality Management

The Agency will establish a dedicated Quality Management (QM) Unit that reports directly to the CDRH Director or Deputy Director and establish a quality management framework for the premarket submission process in CDRH. The Framework will include

infrastructure, senior management responsibility, resource management, lifecycle management, and quality management system evaluation.

At least once per year, the Agency will discuss with industry the specific areas it intends to incorporate in its ongoing audit plan. FDA will identify, with industry input, areas to audit, which will include the effectiveness of CDRH's CAPA process. FDA will expand the scope of its annual audits as it implements and builds up its auditing capability. As part of these ongoing audits, high-performing premarket review processes utilized in one division will be identified and shared accordingly with other divisions to improve efficiencies and effectiveness. At a minimum, FDA audits in the following areas will be completed by the end of FY 2020: Deficiency Letters and Pre-Submissions. Additional audits in the following areas will be completed by the end of FY 2022: Submission Issue Meetings, Interactive Review, Withdrawals and Special 510(k) conversions.

The effectiveness of the QM framework will be evaluated in Phase 2 of the Independent Assessment (see Section V).

B. 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 premarket review program to improve consistency. The Agency will also apply user fee revenues to enhance and supplement scientific review capacity by hiring device application reviewers as well as leveraging external experts needed to assist with the review of device applications.

To ensure such additional positions are filled by qualified experts, the Agency will apply user fee revenues to recruitment and hiring. The Agency will apply user fee revenues to retain high-performing supervisors in the premarket review program.

CDRH intends to enter into an Inter-Agency Agreement (IAA) with the Office of Personnel Management (OPM) to provide supplemental recruitment and staffing support throughout MDUFA IV to augment existing FDA Human Resources services.

C. IT Infrastructure for Submission Management

FDA will enhance IT infrastructure that will allow FDA to perform quality management audits and review consistency.

FDA will implement a new information management system that provides an industry dashboard that displays near real-time submission status.

FDA will develop electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review process. By FY 2020, the Agency will issue a draft guidance document on the use of the electronic submission templates. FDA will provide an opportunity for

public comment on the guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement the guidance once final. In addition, the Agency will update the Guidance "eCopy Program for Medical Device Submissions" to reflect the respective changes to the technical standards and specifications.

FDA will link pre-submissions with subsequent premarket submissions when identified by the applicant.

D. Training

FDA will continue to improve training for new and existing reviewers under this agreement. FDA will achieve Kirkpatrick Level 3 for curriculum-based premarket training through assessment of work performance behavior change and evaluate the effectiveness of the impact of curriculum-based premarket training activities on relevant premarket program metrics and goals (Kirkpatrick Level 4) by the end of FY 2020. FDA training efforts will also be closely coordinated with the Quality Management Unit described in item III.A above to provide more targeted and personalized training to staff.

E. Time Reporting

FDA will implement complete time reporting by the end of MDUFA IV such that data from time reporting can be used to conduct workload analysis and capacity planning.

F. Fee Setting, Fee Collections, and Workload

FDA will seek authority to eliminate the fifth-year offset provision and to maintain and use any and all fee collections, including collections over the statutory total revenue targets.

If the collections are in excess of the resources needed to meet performance goals given the workload, or in excess of inflation-adjusted statutory revenue targets, FDA and industry will work together to assess how best to utilize those resources to improve performance on submission types with performance goals and/or quality management programs, using, as input for the discussion: workload information, performance objectives and ongoing reported performance.

IV. Process Improvements

A. 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 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 and is expected to support reductions in total time to decision. The interactive review process contemplates increased informal interaction between FDA and applicants, including the exchange of scientific and regulatory information.

B. Deficiency Letters

By October 1, 2017, the Agency will publish a level 2 update to the final guidance "Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA; Final Guidance for Industry and FDA Staff" to reflect the following:

All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a marketing authorization decision (e.g., 510(k) clearance, PMA approval, and de novo classification). Any additional best practices identified by quality audits and/or the Independent Assessment will be incorporated in updates to the guidance, as appropriate.

FDA will train staff and managers on this process improvement and the updated guidance.

C. Device Accessories

FDA and Industry will explore additional mechanisms for a streamlined, resource minimal pathway to reclassify accessories previously classified as class III devices as a part of a PMA review if they meet the requirements of a low or moderate risk device.

D. Enhanced Use of Consensus Standards

FDA will establish an Accreditation Scheme for Conformity Assessment (ASCA) Program using FDA-recognized consensus standards. FDA will define the 'scheme' and oversee the Conformity Assessment (CA) model and ensure that there is appropriate interaction with parties that serve as Accrediting Bodies (ABs) for the Certification Bodies (CBs) to certify test laboratories (TLs). When a device type using the 'scheme' is

evaluated according to a specific recognized standard by a certified TL, FDA intends to rely on the certification for the purpose of premarket review, i.e., to treat certifications like full Declarations of Conformity without the need to address further questions related to standards conformance. Assuming that it meets established criteria as outlined in the ASCA program, a device company's internal TL will be eligible to participate in the ASCA program. FDA will not review reports from certified TLs except as part of a periodic quality audit or if FDA becomes aware of new information materially relevant to safety and/or effectiveness.

Specific actions that FDA will undertake include the following:

1. Conduct a Public Workshop by the end of FY 2018 to discuss objectives for the establishment of ABs and CBs. Discussion would include areas (specific FDA-recognized consensus standards) where the ASCA Program can be piloted to maximize initial impact of existing CA activities and potential new areas.
2. Hold educational sessions with stakeholders by the end of FY 2018 about the purpose of the ASCA Program
3. Develop and initiate the pilot of the ASCA program with stakeholder input by the end of FY 2020.
    a. FDA intends to pilot inclusion of recognized standards of public health significance where specific pass/fail criteria are part of the standard
4. Develop an internal IT system to track CA activities of the ASCA Program
5. Establish a process for accreditation of ABs, CBs and/or TLs. FDA will issue draft guidance by the end of FY 2019 and issue final guidance within 12 months post initiation of the pilot.
    a. In limited circumstances, the FDA may directly accredit third-party CBs. For example, FDA could directly accredit third party CBs, if FDA has not identified and recognized an AB within 2 years after establishing the tenets of the ASCA program.
6. Establish a process for reaccreditation and the suspension or withdrawal of accreditation of poor performing ABs, CBs and/or TLs. FDA will issue draft guidance by the end of FY 2019 and final guidance within 12 months post initiation of the pilot.
7. Establish a publicly-accessible website listing CBs/TLs accredited by ASCA and the FDA-recognized consensus standard(s) for which they are accredited
8. FDA, in consultation with stakeholders, will identify appropriate recognized consensus standards for consideration as part of the pilot as the specific focus for ASCA.
    a. By the end of FY 2022: FDA will have piloted, and provided a report on the viability of, an ASCA program which utilizes the schema identified in guidance to include utilization of 5 appropriate cross-cutting/horizontal and/or device-specific areas, at least one of which will be device-specific.
    b. Standards included as part of the ASCA Program will need to have well established endpoints/acceptance criteria built into the standard to allow effective tracking of TL competence.

FDA will provide an annual report on the progress of the ASCA program.

FDA will work with stakeholders for further input on programmatic improvements and/or consideration for expansion.

E. Third Party Review

The Agency will take the following actions to improve the Third Party Review program with a goal of eliminating routine re-review by FDA of Third Party reviews:

1. Strengthen the process for accreditation of Third Parties.
    a. Provide training for Third Parties seeking accreditation by FDA. This training shall include the opportunity for Third Parties to have access to redacted review memos and other information as appropriate.
    b. When FDA's expectations for a particular device type change, FDA will have in place a process to convey this information to the Third Parties and to industry.
2. By the end of FY 2018, establish a plan for eliminating routine re-review by FDA of Third Party reviews and implement plan within 12 months.
3. Implement a program to audit reviews conducted by accredited Third Parties.
    a. Provide tailored re-training to accredited Third Parties based on the results of audits.
4. By the end of FY 2018, issue draft guidance outlining criteria for reaccreditation of 3rd Parties and the suspension or withdrawal of accreditation of a Third Party. FDA will issue final guidance within 12 months of the conclusion of the public comment period.
5. Publish performance of individual accredited Third Parties with at least five completed submissions on the web (e.g., rate of NSE, average number of holds, average time to SE).
6. Require the independent assessment of the Third Party Review Program to evaluate efficiency including the circumstances when FDA re-reviews were conducted; and to suggest process improvements.

The Agency will seek greater authority to tailor the program. Specifically, FDA intends to expand the scope of the program to some product codes that require clinical data and to remove product codes from eligibility when appropriate, such as if/when safety signals arise.

As resources permit, FDA will identify pilot device areas to be the specific focus of an effort where FDA would work with willing industry partners to ensure that information allowing for high quality Third Party reviews could be made available to provide a proof of concept in certain device areas and enable the development of a broader successful program.

F. Patient Engagement & the Science of Patient Input

The Agency will take the following actions to advance patient input and involvement in the regulatory process. Where appropriate, the Agency will leverage public private partnerships (PPPs) to advance these actions.

1. Develop clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing applicant-proposed use of publicly available and validated, voluntary patient preference information (PPI) or voluntary patient reported outcomes (PROs). These staff will provide submission review and early consultation/advice to industry during study planning.
2. By the end of FY 2020, hold one or more public meetings to discuss the topics below and publish the findings and next steps.
    a. Discuss approaches for incorporating PPI and PRO as evidence in device submissions, as well as other ways of advancing patient engagement;
    b. Discuss ways to use patient input to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention;
    c. Public meetings should include specific examples and case histories for PPIs and PROs to ensure clarity and understanding by workshop attendees; and
    d. Identify priority areas where decisions are preference-sensitive and PPI data can inform regulatory decision-making, in order to advance design and conduct of patient preference studies in high impact areas. Publish the priority areas in the Federal Register for public comment following the public meeting.
3. FDA will undertake several activities to improve the regulatory predictability and impact of PROs, including:
    a. Clarify to device review divisions that use of PROs is voluntary and may be one potential way of demonstrating safety or effectiveness (or elements of either or both, such as in a composite endpoint). Consistent with least burdensome principles, applicants may use alternative approaches.
    b. Modify the guidance to outline a flexible framework for PRO validation evidentiary thresholds. These thresholds may vary depending on the particular regulatory use of the PRO.
    c. Work on developing a model for “bridging studies” to make efficient use of existing validated PROs which may be improved, or adapted to other subpopulations or other regulatory uses in a more streamlined and expeditious manner than creating novel PROs.
4. The existing dispute resolution process should be used in the event of disagreement between the applicant and the Agency on the need for PPI or PRO.

G. Emerging Diagnostics

FDA will work with industry to continue the pilot for emerging diagnostics started under MDUFA III.

H. Real World Evidence (RWE)

1. The Agency will use user fee revenue to support the National Evaluation System for health Technology (NEST) by providing funding for the NEST Coordinating Center and hiring FDA staff with expertise in the use of RWE. The NEST governing board will include no fewer than 4 representatives of the trade associations that participated in the MDUFA IV negotiations (AdvaMed, MDMA, MITA, and ACLA), with each association appointing an individual to serve. Industry representation on the NEST governing board will make up at least 25% of the governing board membership. The representative from each trade association may be part of the staff of the association or appointed from a member company. If any of the trade associations elects not to participate on the NEST governing board or for any additional seats allocated to Industry, the participating trade associations will determine how to fill any vacant Industry positions. By the end of FY2019, NEST will implement pilots for at least two product codes (and related product codes), one of which will cover devices approved through the PMA process and the other of which will cover devices cleared through the 510(k) process. The NEST Coordinating Center will seek ways in which to make NEST financially self-sustaining so as not to rely on MDUFA user fees in the long term unless FDA and Industry determine continued user fee support is warranted and provides a sufficient return on investment.
2. FDA will contract with an organization to serve as the NEST Coordinating Center to facilitate use of real world evidence to support premarket activities. The contract will specify actions the Coordinating Center will take to advance the use of RWE, including:
    a. Establish a framework to fund pilot projects to determine the usability of RWE for:
        i. Expanded indications for use
        ii. New clearances/approvals
        iii. Improved malfunction reporting
    b. No later than October 1, 2020, the Coordinating Center will hold a public meeting to review and evaluate the progress and outcomes (as of the date of the public meeting) of the pilots described in (H)(1) above.
    c. The pilots will take place over a period of three years, including data analysis and the Coordinating Center will issue a publicly available report of the results.
    d. The pilots will include devices not currently subject to a registry.
    e. At the conclusion of the pilots, an independent third-party will conduct an assessment to evaluate the strengths, limitations, and appropriate use of RWE for informing premarket decision-making for multiple device types.

f. If warranted based on the results of the pilot(s) described in (H)(1) above, FDA will revise its guidance on the use of RWE to reflect what has been learned from the pilots as to how RWE can be used to support:
    i. Expanded indications for use; and
    ii. New clearances/approvals.

   If supported by the pilot(s) described in (H)(1) above, the guidance will include discussion of how devices not currently subject to a registry can benefit from RWE.

3. The Agency will establish criteria for streamlining MDR requirements.
    a. For most, if not all, device procodes, FDA will permit manufacturers of such devices in those procodes to report malfunctions on a quarterly basis and in a summary MDR format. FDA will publish the list of eligible device procodes within 12 months of receiving a proposed list from Industry. The list will include, among other device procodes, Class II implantable and Class III devices, as appropriate, and will reflect FDA's consideration of Industry's proposed list.
    b. FDA may determine that devices under a new procode in existence for less than 2 years are not eligible for reporting of malfunctions on a quarterly basis and in a summary format.
    c. If a new type of malfunction occurs that the manufacturer has not previously reported to FDA, the manufacturer must submit an individual report. The manufacturer will notify FDA when the issue has been resolved, using current requirements per 21 C.F.R. §§ 803, 806.
    d. FDA will maintain on its website the list of eligible device procodes for which manufacturers are permitted to report malfunctions on a quarterly basis and in a summary MDR format.
    e. FDA will establish a mechanism at the time it publishes the list of eligible devices under 3(a) that permits stakeholders to request device procodes be added to the list.
    f. Nothing in this section precludes the Agency from requiring individual malfunction reports from a specific manufacturer and/or for a specific device if necessary to protect public health. In these situations, FDA will notify the manufacturer they are not eligible for quarterly summary MDR reporting and provide an explanation for that decision and the steps necessary to return to eligibility for quarterly summary MDR reporting.
4. FDA will not require postmarket surveillance studies (i.e., 522 Studies) for devices for which registries and/or other real world data (RWD) sources exist if FDA has access to the information/data in the RWD source and has determined that the information/data in the RWD source is sufficient to take the place of a postmarket surveillance study.

I. Digital Health

The Agency will build expertise and streamline and align FDA review processes with software lifecycles for Software as a Medical Device (SaMD) and software inside of medical devices (SiMD). Specifically, the Agency will:

1. Establish a central digital health unit within CDRH's Office of the Center Director to ensure proper coordination and consistency across the Agency. The Agency will not reorganize staff such that existing review staff would be reassigned to the central digital health unit, while retaining and not disrupting the existing digital health talent within the reviewing divisions who have established, long-term therapeutic and device expertise. The digital health unit will perform, at a minimum, the following tasks:
    a. Develop software and digital health technical expertise ("Technical Experts") to provide assistance for premarket submissions that include SaMD, SiMD, interoperable devices, or otherwise incorporate novel digital health technologies.
    b. Utilize Technical Experts as appropriate or when requested by the manufacturer for submissions that include SaMD, SiMD, interoperable devices, or otherwise incorporate novel digital health technologies; and
    c. Incorporate appropriate metrics for digital health improvements to monitor, track, analyze and report the results of digital health premarket review timelines.
2. Publish final guidance addressing when to submit a 510(k) for a software modification to an existing device within 18 months of the close of the comment period.
3. Explore opportunities to establish premarket approval/clearance pathways tailored to SaMD, SiMD, and novel digital health technologies that take into account real world evidence while incorporating principles established through international harmonization. To accomplish this task, the Agency will:
    a. Engage with stakeholders, including industry, through roundtables, informal meetings, and teleconferences;
    b. Hold a public workshop; and
    c. Revise existing and/or publish new relevant guidance documents, including publishing a draft revised version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (issued in 2005) by the end of FY2019, and within 12 months of the close of the comment period, publish the final revised version. The Agency will incorporate applicable concepts from its Guidance for "Off-The-Shelf Software Used in Medical Devices."
4. Participate in international harmonization efforts related to digital health, including work on developing SaMD and other digital health convergence efforts through the International Medical Device Regulators Forum (IMDRF).

J. Guidance Document Development

FDA will apply user fee revenues to ensure timely completion of Draft Guidance documents. The Agency will strive to finalize, withdraw, reopen the comment period, or issue a new draft guidance for 80% of draft guidance documents within 3 years of the close of the comment periods as resources permit. The Agency will strive to finalize, withdraw, reopen the comment period, or issue a new draft guidance for 100% of draft guidance documents within 5 years of the close of the comment periods as resources permit. The Agency will continue to develop guidance documents and improve the development process as resources permit, but not to the detriment of meeting quantitative review timelines and statutory obligations.

K. Total Product Life Cycle (TPLC)

The establishment of CDRH's Office of In Vitro Diagnostic Device Evaluation and Safety (now the Office of In Vitro Diagnostics and Radiological Health (OIR)) has led to improved consistency and predictability due to the enhanced integration of premarket, postmarket, and compliance-related activities and staff and improved information sharing among staff. In addition, the successful development and evaluation of medical devices depends on the integration of clinical with scientific and engineering disciplines. CDRH will explore transitioning to a similar TPLC model building in the other device areas based on the lessons learned from its experience with OIR and taking into account the Center's mission, vision, strategic priorities, and development of a patient-centric benefit-risk framework for regulatory and non-regulatory decision making across the TPLC. Because an essential element for the success of the Center's benefit-risk decision making framework and approach to device regulation (particularly emerging and innovative technologies) is the incorporation of the clinical context and the impact of a decision on patient health and quality of life, CDRH will take steps to increase and enhance the integration of its clinicians into its TPLC activities, amongst themselves, and with the Center's scientists and engineers. Building on the success of considering and incorporating additional expertise and viewpoints into our decision-making, such as through the use of the Network of Experts and the leveraging of patient perspectives, CDRH will also explore ways in which to better learn from and leverage the expertise of clinicians in other parts of the agency and outside of the agency to inform its decision making, enhance consistency, and assure a more holistic clinical perspective. Clinicians involved in device-related activities will have appropriate training on and make recommendations consistent with applicable device statutory provisions, regulations, guidances, and this Commitment Letter. In addition, CDRH will provide managerial oversight of clinician recommendations and device submission decisions, except for those devices subject to CBER oversight.

V. Independent Assessment of Review Process Management

FDA and the 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 within the budget provided under this user fee agreement.

Phase 1

During the first phase, the contractor will complete an evaluation of FDA's implementation of the corrective action plan developed in response to recommendations from the MDUFA III independent assessment.

For Phase 1, FDA will award the contract by the end of CY2017. The contractor will evaluate the implementation of MDUFA III recommendations and publish a written assessment within 1 year of contract award.

Phase 2

During the second phase, the contractor will:

1. Evaluate FDA's premarket review program to identify efficiencies that should be realized as a result of the process improvements and investments under MDUFA III and IV;
2. Evaluate premarket review program infrastructure and allocation of FTEs;
3. Assess the alignment of resource needs with the training and expertise of hires;
4. Identify and share best practices across branches in ODE and OIR;
5. Assess the effectiveness of programs targeted for improvement under this agreement, including the:
    a. Quality Management program,
    b. Proportion of deficiencies in which FDA references the basis for the deficiency determination,
    c. Pre-Submission program (assess whether (a) CDRH is providing guidance specific to the questions being asked; (b) CDRH is using Pre-Submissions appropriately; and (c) CDRH and Industry are adhering to the procedural aspects as set forth in this agreement),
    d. Third Party Review program (assess efficiency of program and suggest process improvements),
    e. Digital Health program,
    f. Patient Engagement program, and
    g. Real World Evidence program;

6. Analyze conversions of Special 510(k)s to Traditional 510(k)s; and
7. Assess other key areas identified by FDA and industry as resources permit.

For Phase 2 of the independent assessment, FDA will award the contract no later than 3/31/2020. However, the contractor would not begin the audit of deficiency letters and Pre-Submissions before 10/1/2020. The contractor will publish comprehensive findings and recommendations within 1 year. For all recommendations the contractor will provide an estimate of additional resources needed or efficiencies gained, as applicable.

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 and, as appropriate, develop and implement a corrective action plan, and assure its effectiveness.

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 IV, 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 that do not go through a 3rd party, 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 de novo requests, reporting will include:
     - i. Average, and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision
     - ii. Average number of review cycles.
     - iii. Rate of submissions not accepted for review, upon final guidance

1.4. For Pre-Submissions, reporting will include:
   i. Number of all qualified Pre-Submissions received
   ii. Rate of submissions not accepted for review, upon final guidance
   iii. Average and quintiles of the number of calendar days from submission to written feedback
   iv. Number of Pre-Submissions that require a meeting
   v. Percent of submissions with meetings for which industry provided minutes within 15 days

1.5. 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

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), de novo, and PMA submissions
   2.3. Rate of Not Approvable decisions for PMA submissions
   2.4. Rate of Denial decisions for de novo requests
   2.5. 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
   2.6. Specific topic or product area as it relates to performance goals, agreed upon at the previous meeting
   2.7. Number of submissions that missed the goals and the total number of elapsed calendar days broken down into FDA days and industry days
   2.8. Newly released draft and final guidance documents, and status of other priority guidance documents
   2.9. Agency level summary of fee collections
   2.10. Independent assessment implementation plan status
   2.11. Results of independent assessment and subsequent periodic audits and progress toward implementation of the recommendations and any corrective action
   2.12. 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 510(k) submissions that go through a 3rd party, reporting will include:
- i. Time from FDA receipt of third party report to FDA decision at the 90% percentile
- ii. Once 3rd party program enhancements have been implemented, resources saved as a result of enhancements to the 3rd party review program.

3.8. 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
- viii. Number of submissions FDA classifies as unsolicited major, solicited major, and minor amendments

3.9. For De Novo requests, reporting will include:
- i. Number of submissions received
- ii. Average and number of days to Accept/Refuse to Accept, upon final guidance

3.10. 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

3.11. Report on the ASCA program

3.12. Data regarding the reduction in reviewer to manager ratio.

3.13. Report on implementation of deficiency performance improvements.

3.14. Report on quality management program

3.15. Summary of quality system audits

FDA will report annual and quarterly data on performance within goals for 510(k), de novo, and PMA MDUFA decisions for devices identified as LDTs by the submitter compared to all non-LDT IVD devices. The following elements will be reported:

- Number and percentage of LDT 510(k)s and non-LDT IVD 510(k)s completed within 90 FDA days
- Number and percentage of LDT de novos and non-LDT IVD de novos completed within 150 FDA days
- Number and percentage of LDT PMAs and non-LDT IVD PMAs completed within 180 FDA days

FDA commits to treat LDTs no less favorably than other devices to which MDUFA performance goals apply.

On an annual basis, FDA and Industry will discuss the return on investment, which may include process improvements, improved performance, and other enhancements, under MDUFA IV.

VII. 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 of the Federal Food, Drug, and Cosmetic Act (FDCA);
- a premarket notification under section 510(k) of the FDCA;
- an application for investigational device exemption under section 520(g) of the FDCA;
- a Pre-Submission;
- a *de novo* request (evaluation of automatic class III designation) under section 513(f)(2) of the FDCA;
- a CLIA Waiver by application.

B. Electronic Copy (e-Copy)

An electronic copy is an exact duplicate of a 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. Electronic submission template

An electronic submission template, or eSubmission template, is a guided submission preparation tool for industry. Similar to an online form, the eSubmission template walks industry through the relevant contents and components for the respective premarket submission type and device in order to facilitate submission preparation and enhance consistency, quality, and efficiency in the premarket review process.

D. 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 de novo classification request), filed (PMA) or submitted (CLIA Waiver by application). 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).

E. 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).

De Novo Requests: Decisions for *De Novo* requests are grant, withdrawal, and decline.

CLIA Waiver by Application Submissions: Decisions for CLIA Waiver by Application Submissions are Approval, Withdrawal, and Denial.

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

F. 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 testing protocols or data requirements; design and performance of clinical studies and acceptance criteria). 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.

- 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).

- General information requests initiated through the Division of Industry and Consumer Education (DICE).

- 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.

G. 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.

H. 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 average 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 FY2018, the average Total Time to Decision for PMA applications would be the average of FY2016 through FY2018) 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.

I. Accreditation Scheme for Conformity Assessment

Accreditation is the formal recognition by an independent body, generally known as an accreditation body, that a certification body is capable of carrying out certification. Accreditation is not obligatory but it adds another level of confidence, as 'accredited' means the certification body has been independently checked to make sure it operates according to international standards.

Certification Body possesses the necessary competence and other qualifications to sponsor and operate a certification program. A certification body is that organization

under whose authority a certification program is developed and operated and conducts the certification of conformity. Note: A certification body may operate its own testing and inspection activities or oversee these activities carried out on its behalf by other bodies, such as a testing laboratory.

Certification Scheme is the conformity assessment system related to management systems to which the same specified requirements, specific rules and procedures apply.

Conformity Assessment is the demonstration that specified requirements relating to a product, process, system, person or body are fulfilled.

Testing laboratory is an organization that carries out the conformity assessment process.

Third-party Conformity Assessment Activity is a conformity assessment activity that is performed by a person or body that is independent of the person or organization that provides the object, and of user interests in that object.

J. 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.