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PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2028 THROUGH 2032

This document contains the performance goals and procedures for the Prescription Drug User Fee Act (PDUFA) reauthorization for fiscal years (FYs) 2028-2032, known as PDUFA VIII. It is commonly referred to as the "goals letter" or "commitment letter." The goals letter represents the product of FDA's discussions with the regulated industry and public stakeholders, as mandated by Congress. The performance and procedural goals and other commitments specified in this letter apply to aspects of the human drug review program that are important for facilitating timely access to safe, effective, and innovative new medicines for patients. While much of FDA's work is associated with formal tracked performance goals, the Agency and the regulated industry mutually agree that it is appropriate to manage some areas of the human drug review program with internally tracked timeframes. This provides FDA the flexibility needed to respond to a highly diverse workload, including unanticipated public health needs. FDA is committed to meeting the performance goals specified in this letter and to continuous improvement of its performance regarding other important areas specified in relevant published documents[1] that relate to preapproval drug development and post-approval activities for marketed products. FDA and the regulated industry will periodically and regularly assess the progress of the human drug review program throughout PDUFA VIII. This will allow FDA and the regulated industry to identify emerging challenges and develop strategies to address these challenges to ensure the efficiency and effectiveness of the human drug review program.

Unless otherwise stated, goals apply to cohorts of each fiscal year (FY).

[1] Refer to the Good Review Management Principles and Practices for PDUFA Products guidance (hereinafter referred to as "GRMP guidance") and the Good Review Management Principles and Practices for Effective IND Development and Review MAPP (hereinafter referred to as "GRMP MAPP").

I. ENSURING THE EFFECTIVENESS OF THE HUMAN DRUG REVIEW PROGRAM

A. REVIEW PERFORMANCE GOALS

1. Review and Act on NDA/BLA Submissions and Resubmissions[2] According to the Following Timelines and Goals.

Table 1: Performance Goals for NDA/BLA Submissions and Resubmissions

SUBMISSION COHORT	STANDARD	PRIORITY
NME NDAs and original BLAs	90% in 10 months of the 60-day filing date	90% in 6 months of the 60-day filing date
Non NME NDAs	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmissions[3]	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmissions	90% in 6 months of the receipt date	90% in 6 months of the receipt date
Original Efficacy Supplements	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmitted Efficacy[4] Supplements	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmitted Efficacy Supplements	90% in 6 months of the receipt date	90% in 6 months of the receipt date

Table 2: Performance Goals for Manufacturing Supplements

SUBMISSION COHORT	PRIOR APPROVAL	ALL OTHER
Manufacturing Supplements	90% in 4 months of the receipt date	90% in 6 months of the receipt date

[2] Refer to section I.B for a description of the review program for NME NDAs and original BLAs.
[3] FDA will report the number filed, on time, and overdue for Class 1 & Class 2 resubmitted original applications separately, but for review goal performance purposes (percentage on time), these will be consolidated into one performance goal.
[4] FDA will report the number received, on time, and overdue for Class 1 & Class 2 resubmitted efficacy supplements separately, but for review goal performance purposes (percentage on time), these will be consolidated into one performance goal.

2. Review Performance Goal Extensions

a. Major Amendments

i. A major amendment to an original application, efficacy supplement, or resubmission of any of these applications, submitted at any time during the review cycle, may extend the goal date by three months.

ii. A major amendment may include, for example, a major new clinical safety/efficacy study report; major re-analysis of previously submitted study(ies); submission of a Risk Evaluation and Mitigation Strategy (REMS) with Element to Assure Safe Use (ETASU) not included in the original application; or significant amendment to a previously submitted REMS with ETASU. Generally, changes to REMS that do not include ETASU and minor changes to REMS with ETASU will not be considered major amendments.

iii. A major amendment to a manufacturing supplement submitted at any time during the review cycle may extend the goal date by two months.

iv. Only one extension can be given per review cycle.

v. Consistent with the underlying principles articulated in the GRMP guidance, FDA's decision to extend the review clock should, except in rare circumstances, be limited to occasions where review of the new information could address outstanding deficiencies in the application and lead to approval in the current review cycle.

b. Inspection of Facilities Not Adequately Identified in an Original Application or Supplement

i. All original applications, including those in the "Program," (see section I.B.2) and supplements are expected to include a comprehensive and readily located list of all manufacturing facilities included or referenced in the application or supplement. This list provides FDA with information needed to schedule inspections of manufacturing facilities that may be necessary before approval of the original application or supplement.

ii. If, during FDA's review of an original application or supplement, the Agency identifies a manufacturing facility that was not included in the comprehensive and readily located list, the goal date may be extended.

1) If FDA identifies the need to inspect a manufacturing facility that is not included as part of the comprehensive and readily located list in an original application or efficacy supplement, the goal date may be extended by three months.

2) If FDA identifies the need to inspect a manufacturing facility that is not included as part of the comprehensive and readily located list in a manufacturing supplement, the goal date may be extended by two months.

c. Extensions Following a Post-PAI or Post-PLI Meeting for Original NDAs or BLAs, Not Including Supplements

i. When a meeting request package containing substantive information related to a response to deficiencies observed on a PAI or PLI is submitted prior to a post-PAI or post-PLI meeting, or substantive information is provided to FDA following a post-PAI or post-PLI meeting, FDA may extend the goal date by 3 months.

ii. FDA's decision to extend the review clock should, except in rare circumstances, be limited to occasions when an extension would permit review of the new information provided, and there is a reasonable likelihood that review of the new information provided could address outstanding facility deficiencies relevant to the application and lead to approval in the current review cycle.

iii. Only one extension will be afforded per review cycle, inclusive of extensions for Major Amendments and for Inspection of Facilities Not Adequately Identified in an Original Application or Supplement.

B. PROGRAM FOR ENHANCED REVIEW TRANSPARENCY AND COMMUNICATION FOR NME NDAs AND ORIGINAL BLAs

To promote transparency and communication between the FDA review team and the applicant, FDA will apply the following model ("the Program") to the review of all New Molecular Entity New Drug Applications (NME NDAs) and original Biologics License Applications (BLAs), including applications that are resubmitted following a Refuse-to-File decision, received from October 1, 2027, through September 30, 2032.[5] The goal of the Program is to promote the efficiency and effectiveness of the first cycle review process and minimize the number of review cycles necessary for approval, ensuring that patients have timely access to safe, effective, and high quality new drugs and biologics.

Approach to Application Review: The standard approach for the review of NME NDAs and original BLAs is described in this section. However, the FDA review team and the applicant may discuss and reach mutual agreement on an alternative approach to the timing and nature of interactions and information exchange between the applicant and FDA, i.e., a Formal Communication Plan for the review of the NME NDA or original BLA. The Formal Communication Plan may include elements of the standard approach (e.g., a mid-cycle communication or a late-cycle meeting) as well as other interactions that sometimes occur during the review process (e.g., a meeting during the filing period to discuss the application, i.e., an "application orientation meeting"). If appropriate, the Formal Communication Plan should specify those elements of the Program that FDA and the applicant agree are unnecessary for the application under review. If the review team and the applicant anticipate developing a Formal Communication Plan, the elements of the plan should be discussed and agreed to at the pre-submission meeting (see section I.B.1) and reflected in the meeting minutes. The Formal Communication Plan may be reviewed and amended at any time based on the progress of the

[5] The decision as to whether the application is included or excluded from the Program is distinct from FDA's determination as to whether the drug product contains a "new chemical entity," as defined under 21 CFR 314.108(a). Determinations regarding new chemical entity exclusivity are made at the time of approval of an application.

review and the mutual agreement of the review team and the applicant. For example, the review team and the applicant may mutually agree at any time to cancel future specified interactions in the Program (e.g., the late-cycle meeting) that become unnecessary (e.g., because previous communications between the review team and the applicant are sufficient). Any amendments made to the Formal Communication Plan should be consistent with the goal of an efficient and timely first cycle review process and not impede the review team's ability to conduct its review.

The remainder of section I.B describes the parameters that will apply to FDA's review of applications in the Program.

1. **Pre-Submission Meeting:** The applicant is strongly encouraged to discuss the planned content of the application with the appropriate FDA review division at a pre-NDA/BLA meeting. This meeting will be attended by the FDA review team, including appropriate senior FDA staff.

    a. The pre-NDA/BLA meeting should be held sufficiently in advance of the planned submission of the application to allow for meaningful response to FDA feedback and should generally occur not less than 2 months prior to the planned submission of the application.

    b. In addition to FDA's preliminary responses to the applicant's questions, other potential discussion topics include preliminary discussions on the need for REMS or other risk management actions, and, where applicable, the development of a Formal Communication Plan and a timeline for review activities associated with a scheduling recommendation under the Controlled Substances Act for drugs with abuse potential. These discussions will be summarized at the conclusion of the meeting and reflected in the FDA meeting minutes.

    c. The FDA and the applicant will agree on the content of a complete application for the proposed indication(s) at the pre-submission meeting. The FDA and the applicant may also reach agreement on submission of a limited number of application components not later than 30 calendar days after the submission of the original application. These submissions must be of a type that would not be expected to materially impact the ability of the review team to begin its review. These agreements will be summarized at the conclusion of the meeting and reflected in the FDA meeting minutes.

        i. Examples of application components that may be appropriate for delayed submission include updated stability data (e.g., 15-month data to update 12-month data submitted with the original submission) or the final audited report of a preclinical study (e.g., carcinogenicity) where the final draft report is submitted with the original application.

        ii. Major components of the application (e.g., the complete study report of a Phase 3 clinical trial, or the full study report of required long-term safety data) are expected to be submitted with the original application and are not subject to agreement for late submission.

2. **Original Application Submission:** Applications are expected to be complete, as agreed between the FDA review team and the applicant at the pre-NDA/BLA meeting, at the time of original submission of the application. If the applicant does not have a pre-NDA/BLA meeting with FDA, and no agreement exists between FDA and the applicant on the contents of a complete application or delayed submission of certain components of the application, the applicant's submission is expected to be complete at the time of original submission.

    a. All applications are expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities included or referenced in the application.

    b. Any components of the application that FDA agreed at the pre-submission meeting could be submitted after the original application are expected to be received not later than 30 calendar days after receipt of the original application.

    c. Incomplete applications, including applications with components that are not received within 30 calendar days after receipt of the original submission, will be subject to a Refuse-to-File decision.

    d. The following parameters will apply to applications that are subject to a Refuse-to-File decision and are subsequently filed over protest:

        i. The original submission of the application will be subject to the review performance goal as described in section I.B.4.

        ii. The application will not be eligible for the other parameters of the Program (e.g., mid-cycle communication, late-cycle meeting).

        iii. FDA generally will not review amendments to the application during any review cycle. FDA also generally will not issue information requests to the applicant during the Agency's review.

        iv. The resubmission goals described in sections I.A.1 will not apply to any resubmission of the application following an FDA complete response action. Any such resubmission will be reviewed as available resources permit.

    e. Since applications are expected to be complete at the time of submission, unsolicited amendments are expected to be rare and not to contain major new information or analyses. Review of unsolicited amendments, including those submitted in response to an FDA communication of deficiencies, will be handled in accordance with the GRMP guidance. This guidance includes the underlying principle that FDA will consider the most efficient path toward completion of a comprehensive review that addresses application deficiencies and leads toward a first cycle approval when possible.

3. **Day 74 Letter:** FDA will follow existing procedures regarding identification and communication of filing review issues in the "Day 74 letter." For applications subject to the Program, the timeline for this communication will be within 74 calendar days from the date of FDA receipt of the original submission. The planned review timeline included in the Day 74 letter for applications in the Program will include the planned date for the

internal mid-cycle review meeting, and a target date for communicating labeling consistent with FDA MAPPs and SOPPs.[6] The letter will also include preliminary plans on whether to hold an Advisory Committee (AC) meeting to discuss the application. If applicable, the Day 74 letter will serve as notification to the applicant that the review division intends to conduct an expedited review (See section I.D).

4. **Review Performance Goals:** For NME NDA and original BLA submissions that are filed by FDA under the Program, the PDUFA review clock will begin at the conclusion of the 60-day filing review period that begins on the date of FDA receipt of the original submission. The review performance goals for these applications are as follows:

    a. Review and act on 90 percent of standard NME NDA and original BLA submissions within 10 months of the 60-day filing date.

    b. Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60-day filing date.

5. **Mid-Cycle Communication:** The FDA Regulatory Project Manager (RPM), and other appropriate members of the FDA review team (e.g., Cross Discipline Team Leader (CDTL)), will call the applicant, generally within 2 weeks following the Agency's internal mid-cycle review meeting, to provide the applicant with an update on the status of the review of their application. An agenda will be sent to the applicant prior to the mid-cycle communication. Scheduling of the internal mid-cycle review meeting will be handled in accordance with the GRMP guidance. The RPM will coordinate the specific date and time of the telephone call with the applicant.

    a. The update should include any significant issues identified by the review team to date, any information requests, information regarding major safety concerns and preliminary review team thinking and rationale regarding:

        i. risk management,

        ii. the potential need for any post-marketing requirement(s) (PMRs), and

        iii. the ability of adverse event reporting and FDA's Active Risk Identification and Analysis (ARIA) system under the Sentinel Initiative to provide sufficient information about product risk.

    b. The update should also include proposed date(s) for the late-cycle meeting, updates regarding plans for the AC meeting (if an AC meeting is anticipated), an update regarding FDA's review activities associated with a scheduling recommendation under the Controlled Substances Act (if applicable), and other projected milestone dates for the remainder of the review cycle.

    c. In the case of an expedited review, FDA will communicate the timelines for the Late-Cycle Meeting and the Late-Cycle Meeting background package (see section I.B.6)

[6] FDA will update relevant MAPPs and SOPPs to reflect current practice for communicating labeling.

which may occur earlier with more condensed timeframes compared to a review that is not expedited.

6. **Late-Cycle and Advisory Committee Meetings:** A meeting will be held between the FDA review team and the applicant to discuss the status of the review of the application late in the review cycle. Late-cycle meetings will generally be face-to-face meetings; however, the meeting may be held by teleconference if FDA and the applicant agree. Since the application is expected to be complete at the time of submission, FDA intends to complete primary and secondary reviews of the application in advance of the planned late-cycle meeting.

    a. FDA representatives at the late-cycle meeting are expected to include the signatory authority for the application, review team members from appropriate disciplines, and appropriate team leaders and/or supervisors from disciplines for which substantive issues have been identified in the review to date.

    b. For applications that will be discussed at an AC meeting, the following parameters apply:

        i. FDA intends to convene AC meetings no later than 2 months (standard review) or no later than 6 weeks (priority review) prior to the PDUFA goal date. The late-cycle meeting will occur not less than 12 calendar days before the date of the AC meeting.

        ii. FDA intends to provide final questions for the AC to the applicant and the AC not less than 2 calendar days before the AC meeting.

        iii. Following an AC Meeting, FDA and the applicant may agree on the need to discuss feedback from the AC for the purpose of facilitating the remainder of the review. Such a meeting will generally be held by teleconference without a commitment for formal meeting minutes issued by the Agency.

    c. For applications that will not be discussed at an AC meeting, the late-cycle meeting will generally occur not later than 3 months (standard review) or two months (priority review) prior to the PDUFA goal date.

    d. Late-Cycle Meeting Background Packages: The Agency background package for the late-cycle meeting will be sent to the applicant not less than 10 calendar days (or 2 calendar days for an expedited review) before the late-cycle meeting. The package will consist of a brief memorandum from the review team outlining substantive application issues (e.g., deficiencies identified by primary and secondary reviews), the Agency's background package for the AC meeting (incorporated by reference if previously sent to the applicant), potential questions and/or points for discussion for the AC meeting (if planned) and the current assessment of the need for REMS or other risk management actions. If the application is subject to an expedited review, the background package may be streamlined using a bulleted list to identify issues to be discussed.

    e. Late-Cycle Meeting Discussion Topics: Potential topics for discussion at the late-cycle meeting include major deficiencies identified to date; issues to be discussed at

the AC meeting (if planned); current assessment of the need for REMS and current assessment of the sufficiency of adverse event reporting and the ARIA system to provide information on product risk and the rationale for potential need for a PMR to characterize product risk or other risk management actions; status update of FDA's review activities associated with a scheduling recommendation under the Controlled Substances Act, if applicable; information requests from the review team to the applicant; and additional data or analyses the applicant may wish to submit.

i. With regard to submission of additional data or analyses, the FDA review team and the applicant will discuss whether such data will be reviewed by the Agency in the current review cycle and, if so, whether the submission will be considered a major amendment and trigger an extension of the PDUFA goal date.

ii. With regard to information requests (IRs) that need to be sent from the review team to the applicant after the Late-Cycle Meeting, a description of the issue that triggered the IR will be included to provide context for the applicant when gathering the requested information.

7. **Inspections:** FDA's goal is to complete all GCP, GLP, and GMP inspections for applications in the Program within 6 months of the date of original receipt for priority applications and within 10 months of the date of original receipt for standard applications. This will allow 2 months at the end of the review cycle to attempt to address any deficiencies identified by the inspections.

C. ASSESSMENT OF THE PROGRAM, EFFICACY SUPPLEMENTS, AND COMMUNICATIONS

Beginning in FY 2028 and continuously through the end of the assessment, FDA will contract with an independent third party with expertise in assessing the quality and efficiency of the biopharmaceutical development and regulatory review programs to assess first cycle review processes, outcomes, and FDA-sponsor communications during first cycle review. For NME NDAs and original BLAs submitted during PDUFA VII and PDUFA VIII, the third party will quantify first cycle review outcomes (e.g., approval, complete response) and the timing of the review outcomes, as well as major amendments resulting in review clock extensions.

The third party will assess the completeness, consistency, and timing of key review process milestones, communications, and materials exchanged between FDA and sponsors during IND and NDA/BLA review, especially how, when, and whether significant issues were identified, communicated, and addressed. The third party will also assess adherence to key process milestones as documented within relevant FDA MAPPs, SOPPs, and this letter. For complete response outcomes and major amendments, the third party will summarize the basis for these outcomes and characterize significant review and/or process issues.

The third party will assess trends in complete response rates over time and identify any correlations between first cycle review outcomes and timelines (including clock extensions) and review practices and communications. Key communications will include information requests, feedback on sponsor-submitted materials, labeling comments, and formal meetings and letters. Through these analyses, the third party will identify trends and summarize best practices from across CDER and CBER review offices and divisions.

In addition to the topics above, the third party will evaluate labeling communications between sponsors and FDA during first cycle review (including, e.g., first communication, substantially complete, and last) for a representative sample of efficacy supplements in order to determine the efficiency of the labeling communication process. No other metrics shall be assessed for efficacy supplements.

Finally, the third party will evaluate communications related to pivotal protocols during development. The evaluation will be conducted to assess the elapsed time between submission of a pivotal protocol and FDA's response to questions submitted with the pivotal protocol (and any other FDA comments), whether sponsors consistently provided required information, and the elapsed time from submission of a pivotal protocol to submission of the associated statistical analysis plans (SAP) and time to receipt of relevant FDA comments and questions on the SAP. As with the other components of this evaluation, the third party will identify any correlation between pivotal protocol review practices and timelines and overall review outcomes.

The third party will be expected to collect and analyze data and, for a sample of applications, review communications between FDA and sponsors and conduct interviews with sponsors and review teams. The third party will use the data to provide actionable recommendations to help FDA and sponsors limit first cycle complete responses (for applications that are ultimately approvable), missed goal dates, and review clock extensions. The third party will also provide actionable recommendations to increase the effectiveness of FDA-sponsor communications during review.

Deliverables:

a. Prior to beginning the assessment, FDA will publish the statement of work for this assessment for public comment.

b. By March 31, 2030, FDA and the third party will publish an interim assessment report for public comment.

c. By June 30, 2030, FDA and the third party will hold a public workshop to discuss the interim assessment report. Stakeholders may share feedback on factors affecting first cycle review outcomes and potential strategies for reducing complete responses, missed goal dates, and review clock extensions.

d. By March 31, 2032, FDA and the third party will publish a final report on FDA's public website. This report will include findings from the assessment as well as recommendations for increasing the effectiveness of FDA-sponsor communications and reducing complete responses, missed goal dates, and review clock extensions. The report will also incorporate feedback from the public workshop in section (c).

D. NEW MOLECULAR ENTITY (NME) MILESTONES AND POSTMARKETING REQUIREMENTS (PMRs)

FDA will continue to review, oversee, track, and communicate postmarketing drug safety issues.

1. **Pre-Approval Review of PMRs:** The Agency recognizes the importance of PMRs to ensure the timely availability of information on the safety and efficacy of therapies to the United States public. Therefore, FDA will maintain established processes to support

consistency and predictability for both the Agency and applicants throughout the identification, determination, and evaluation of postmarketing studies.

FDA will continue the following pre-approval process guidelines:

a. For standard NME NDAs and original BLAs, FDA will communicate details on anticipated PMRs required under section 505(o)(3), PREA, Accelerated Approval, and the Animal Rule to the applicant no later than 8 weeks prior to the PDUFA action goal date.

b. For priority NME NDAs and original BLAs, FDA will communicate details on anticipated PMRs required under section 505(o)(3), PREA, Accelerated Approval, and the Animal Rule to the applicant no later than 6 weeks prior to the PDUFA action goal date.

c. The communications described above in clauses (a) and (b) will summarize FDA's preliminary evaluation of required postmarketing studies, including the study purpose, critical study design elements including type of study and study population, timelines for discussions and engagement on the PMR for the remainder of the review cycle, and for 505(o)(3) PMRs the specific serious risk.

d. If a major safety issue which requires a PMR is identified based on data submitted subsequent to submission of the application these timelines may not apply.

FDA's performance goals for **standard** NME NDAs and original BLAs will be as follows:

a. Communicate anticipated PMRs to the applicant no later than 8 weeks prior to the PDUFA action goal date for 80% of standard NME NDAs and original BLAs.

FDA's performance goals for **priority** NME NDAs and original BLAs will be as follows:

a. Communicate anticipated PMRs to the applicant no later than 6 weeks prior to the PDUFA action goal date for 80% of priority NME NDAs and original BLAs.

For the purposes of tracking and reporting metrics on all PMR goals described above, FDA will calculate metrics based on all NME and original BLA applications with issued PMRs, including section 505(o)(3), PREA, Accelerated Approval, and the Animal Rule.

2. **Post-Approval Review of Existing PMRs:** In addition to mechanisms in place for FDA to review existing PMRs (e.g., Annual Status Reports (ASRs), protocol submissions), applicants may also request review of existing PMRs for release. FDA will review sponsor-initiated requests as summarized below:

   a. The applicant will submit a request summarizing their rationale for why an existing PMR is no longer needed, including all necessary supporting data and information.

b. The relevant FDA review division/office[7] and discipline will initiate review of the request. FDA will notify the applicant of any additional information considered necessary to evaluate the request within 45 days of receipt.

c. FDA will respond to the applicant with a decision within 60 days of receipt of the original request or within 60 days of receipt of the additional information requested by FDA described in the previous step, whichever is later. FDA's response can be an agreement letter or a non-agreement letter. In a case of a non-agreement letter, the FDA will provide a rationale for their decision.

d. If FDA's response is a non-agreement letter, the applicant may submit a request to the review division for reconsideration by the appropriate committee(s) described in (e) below with justification, and any additional information, and/or data if appropriate.

e. Upon receipt of a reconsideration request, the review division/office will discuss with the appropriate internal committee that includes senior Agency leadership (e.g., Medical Policy and Program Review Committee, Medical Policy Coordinating Committee, and Pediatric Review Committee).

f. The review division/office will issue a written response within 45 days of receipt of the reconsideration request. FDA's response can be an agreement letter or a non-agreement letter. In a case of a non-agreement letter, the FDA will provide a rationale for their decision.

The process and timelines described above are not PDUFA-tracked metrics or subject to performance goals.

E. EXPEDITED REVIEWS

The term "expedited review" in this letter refers to FDA's review of a human drug application in the Program that has received priority review designation and the FDA review team identifies as meeting an important public health need, where the review team plans to act at least 1 month before the PDUFA goal date provided that no significant application deficiencies prevent an early action. In such cases the FDA review team intends to make every effort to conduct an expedited review and act early on the application. FDA conducts expedited reviews to promote timely access to critically needed therapies for patients without compromising FDA's high standards for demonstrating the safety, efficacy, and quality of new medicines. If significant application deficiencies are identified by the review team at any time during an expedited review, FDA intends to revert, for the remainder of the review, to the normal priority review approach, and will inform the applicant accordingly.

F. REVIEW OF PROPRIETARY NAMES TO REDUCE MEDICATION ERRORS

To enhance patient safety, FDA is committed to various measures to reduce medication errors related to look-alike and sound-alike proprietary names and such factors as unclear label abbreviations, acronyms, dose designations, and error-prone label and packaging design. The

[7] In CDER, initial reviews will be conducted by the relevant review division based on discipline. In CBER, initial reviews will be conducted by the relevant review office based on discipline.

following performance goals apply to FDA's review of drug and biological product proprietary names during development (as early as end-of-phase 2) and during FDA's review of a marketing application:

1. **Proprietary Name Review Performance Goals During Drug Development**

    a. Review 90% of proprietary name submissions filed within 180 days of receipt. Notify sponsor of tentative acceptance or non-acceptance.

    b. If the proprietary name is found to be unacceptable, the sponsor can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).

    c. If the proprietary name is found to be unacceptable, the above review performance goals also would apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.

    d. A complete submission is required to begin the review clock.

2. **Proprietary Name Review Performance Goals During Application Review**

    a. Review 90% of NDA/BLA proprietary name submissions filed within 90 days of receipt. Notify applicant of tentative acceptance/non-acceptance.

    b. A supplemental review will be done meeting the above review performance goals if the proprietary name has been submitted previously (investigational new drug (IND) phase after end-of-phase 2) and has received tentative acceptance.

    c. If the proprietary name is found to be unacceptable, the applicant can request reconsideration by submitting a written rebuttal with supporting data or request a meeting within 60 days to discuss the initial decision (meeting package required).

    d. If the proprietary name is found to be unacceptable, the above review performance goals apply to the written request for reconsideration with supporting data or the submission of a new proprietary name.

    e. A complete submission is required to begin the review clock.

G. MAJOR DISPUTE RESOLUTION

1. Procedure:

For procedural or scientific matters involving the review of human drug applications and supplements (as defined in PDUFA) that cannot be resolved at the signatory authority level (including a request for reconsideration by the signatory authority after reviewing any materials that are planned to be forwarded with an appeal to the next level), the response to appeals of decisions will occur within 30 calendar days of the Center's receipt of the written appeal.

2. Performance Goal:

90% of such answers are provided within 30 calendar days of the Center's receipt of the written appeal.

3. Conditions:

a. Sponsors should first try to resolve the procedural or scientific issue at the signatory authority level. If it cannot be resolved at that level, it should be appealed to the next higher organizational level (with a copy to the signatory authority) and then, if necessary, to the next higher organizational level.

b. Responses should be either verbal (followed by a written confirmation within 14 calendar days of the verbal notification) or written and should ordinarily be to either grant or deny the appeal.

c. If the decision is to deny the appeal, the response should include reasons for the denial and any actions the sponsor might take to persuade the Agency to reverse its decision.

d. In some cases, further data or further input from others might be needed to reach a decision on the appeal. In these cases, the "response" should be the plan for obtaining that information (e.g., requesting further information from the sponsor, scheduling a meeting with the sponsor, scheduling the issue for discussion at the next scheduled available advisory committee (AC)).

e. In these cases, once the required information is received by the Agency (including any advice from an AC), the person to whom the appeal was made again has 30 calendar days from the receipt of the required information in which to either grant or deny the appeal.

f. Again, if the decision is to deny the appeal, the response should include the reasons for the denial and any actions the sponsor might take to persuade the Agency to reverse its decision.

g. If the Agency decides to present the issue to an AC and there are not 30 days before the next scheduled AC, the issue will be presented at the following scheduled committee meeting to allow conformance with AC administrative procedures.

H. CLINICAL HOLDS

1. Procedure:

The Center should respond to a sponsor's complete response to a clinical hold within 30 days of the Agency's receipt of the submission of such sponsor response.

2. Performance Goal:

90% of such responses are provided within 30 calendar days of the Agency's receipt of the sponsor's response.

I. SPECIAL PROTOCOL QUESTION ASSESSMENT AND AGREEMENT

1. Procedure:

Upon specific request by a sponsor (including specific questions that the sponsor desires to be answered), the Agency will evaluate certain protocols and issues to assess whether the design is adequate to meet scientific and regulatory requirements identified by the sponsor.

a. The sponsor should submit a limited number of specific questions about the protocol design and scientific and regulatory requirements for which the sponsor seeks agreement (e.g., is the dose range in the carcinogenicity study adequate, considering the intended clinical dosage; are the clinical endpoints adequate to support a specific efficacy claim).

b. Within 45 days of Agency receipt of the protocol and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the protocol and answers to the questions posed by the sponsor. If the Agency does not agree that the protocol design, execution plans, and data analyses are adequate to achieve the goals of the sponsor, the reasons for the disagreement will be explained in the response.

c. Protocols that qualify for this program include: carcinogenicity protocols, stability protocols, and Phase 3 protocols for clinical trials that will form the primary basis of an efficacy claim. For such Phase 3 protocols to qualify for this comprehensive protocol assessment, the sponsor must have had an end-of-Phase 2/pre-Phase 3 meeting with the review division so that the division is aware of the developmental context in which the protocol is being reviewed and the questions being answered.

d. For products that will be using Subpart E or Subpart H development schemes, the Phase 3 protocols mentioned in this paragraph should be construed to mean those protocols for trials that will form the primary basis of an efficacy claim no matter what phase of drug development in which they happen to be conducted.

e. If a protocol is reviewed under the process outlined above and agreement with the Agency is reached on design, execution, and analyses and if the results of the trial conducted under the protocol substantiate the hypothesis of the protocol, the Agency agrees that the data from the protocol can be used as part of the primary basis for approval of the product. The fundamental agreement here is that having agreed to the design, execution, and analyses proposed in protocols reviewed under this process, the Agency will not later alter its perspective on the issues of design, execution, or analyses unless public health concerns unrecognized at the time of protocol assessment under this process are evident.

2. Performance Goal:

90% of special protocol assessments and agreement requests completed and returned to sponsor within the timeframe.

3. Reporting:

The Agency will track and report the number of original special protocol assessments and resubmissions per original special protocol assessment.

J. PIVOTAL PROTOCOL PRIORITIZATION

During product development when a sponsor submits a pivotal protocol[8] for FDA review, the sponsor will identify the submission as a "Pivotal Protocol" in the subject of the cover letter, and in cases where the protocol may have been previously discussed during a formal meeting or other formal communication with FDA, the date of the meeting or communication will be noted in the cover letter.

When the cover letter identifies the submission as a pivotal protocol, documents the planned study start date, and includes any critical questions requiring responses to enable study initiation, FDA will prioritize review of such protocols consistent with timelines in MAPP 6030.9 and SOPP 8217. FDA will update MAPP 6030.9 and SOPP 8217 by the end of FY 2028 and provide training to review staff to emphasize the prioritization of pivotal protocols.

K. MEETING MANAGEMENT GOALS

1. Formal Meetings:

Formal PDUFA meetings between sponsors and FDA consist of Type A, B, B(EOP), C, Type D and INTERACT meetings. FDA plays an active role during drug development by providing advice and feedback to sponsors on the overall drug development programs during meetings conducted between sponsors and FDA. In general, FDA's guidance provided at these meetings describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. These meetings are further described below.

a. Type A meetings are those meetings that are necessary for an otherwise stalled drug development program to proceed (i.e., a "critical path" meeting) or to address an important safety issue. Post-action meetings requested within three months after an FDA regulatory action other than approval (i.e., issuance of a complete response letter) will also generally be considered Type A meetings.

b. Type B meetings include pre-IND meetings and pre-NDA/BLA meetings, while Type B(EOP) meetings are reserved for certain End-of-Phase 1 meetings (i.e., for 21 CFR Part 312 Subpart E or 21 CFR Part 314 Subpart H or similar products) and End-of-Phase 2/pre-Phase 3 meetings. Meetings regarding REMS or postmarketing requirements that occur outside the context of the review of a marketing application will also generally be considered Type B meetings.

[8] A "pivotal protocol" is defined as a protocol for a study intended to form the primary basis of an efficacy claim for a marketing application.

c. A Type C meeting is any type of meeting[9] other than Type A, B, B(EOP), D, or INTERACT.

d. A Type D meeting is focused on a narrow set of issues (e.g., often one, but typically not more than two issues and associated questions). Requests could include:

   i. A follow-up question that raises a new issue after a formal meeting (i.e., more than just a clarifying question about an FDA response from a prior meeting);

   ii. A narrow issue on which the sponsor is seeking Agency input with only a few associated questions; or

   iii. A general question about an innovative development approach that does not require extensive, detailed advice.

   Type D meetings should be limited to no more than 2 focused topics. If the sponsor has several issues or a complex single issue with multiple questions, a Type C meeting should be requested rather than requesting several Type D meetings. In addition, the issue should not require input from more than 3 disciplines or divisions. If the scope of the meeting is broad or includes complex questions/issues that require input from more than 3 disciplines or divisions, then FDA will inform the sponsor that the Agency will be converting the meeting to the appropriate meeting type (Type B or C) and the sponsor can either withdraw their request or accept the FDA's meeting-type conversion without re-submitting a new meeting request.

e. INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs (INTERACT) meetings are intended for novel questions and unique challenges in early development (i.e., prior to filing of an IND). The issues typically relate to IND requirements for example: questions regarding design of IND-enabling toxicity studies (e.g., species, endpoints), complex manufacturing technologies or processes, development of innovative devices used with a drug or biologic, or the use of cutting-edge testing methodologies. INTERACT meetings are intended to facilitate IND-enabling efforts where the sponsor is facing a novel, challenging issue that might otherwise delay progress of the product towards entry into the clinic in the absence of this early FDA input. Typically, the issue is early in a development program—prior to when a pre-IND meeting might be requested—and the issue may delay initiation of, or progress of, IND-enabling studies. The sponsor needs to have selected a specific investigational product or a product-derivation strategy to evaluate in a clinical study before requesting an INTERACT meeting.

   i. Questions and topics within the scope of an INTERACT meeting include:

      1) Novel questions for all CDER and CBER products (i.e., questions where there is no existing guidance or other information in writing the company could reference from FDA).

[9] Refer to section I.L.2, I.L.3, I.L.5.e, and I.L.5.b of this document that describe specific types of Type C meetings pertaining to new surrogate endpoints, rare disease endpoint development, model informed drug development (MIDD), and complex innovative design (CID), respectively.

2) These meetings are intended to provide FDA input on issues that a sponsor needs to address prior to a pre-IND meeting, including issues such as:

   a) Choice of appropriate preclinical models or necessary toxicology studies for novel drug platforms or drug candidates;

   b) CMC issues or testing strategies aimed to demonstrate product safety, adequate to support first-in-human study;

   c) Overall advice related to the design of proof-of-concept or other pilot safety/biodistribution studies necessary to support administration of an investigational product in a first-in-human clinical trial;

   d) General recommendations regarding a future first-in-human trial in a target clinical population where the population is novel and there is no prior precedent or guidance;

   e) Recommendations on approach for further development of an early-stage product with limited CMC, pharmacology/toxicology, and/or clinical data that were collected outside of a US IND; and

   f) Other topics that would be agreed upon by FDA.

f. When a sponsor is developing an investigational product under multiple INDs across multiple therapeutic areas (e.g., across review divisions), there may be instances when a multi-divisional meeting (MDM) is the most efficient way to address topics of discussion that are broadly applicable to the product.[10] While the primary goal is efficiency, a secondary goal is to seek alignment across participating divisions whenever possible.

   A sponsor may submit an MDM request within the existing formal PDUFA meeting types. The request should be sent simultaneously to all relevant review divisions and should propose a lead division. FDA will target a timeline for responding to requests for an MDM no later than 7 days beyond the response times listed in Table 3. FDA will target a timeline for scheduling an MDM no later than 14 days beyond the times listed in Table 4. MDMs will not be included in FDA performance metrics; however, they will be evaluated as part of a third-party assessment which will look at several metrics, including FDA's timing for response and scheduling of MDMs.

2. Responses to Meeting Requests

a. **Procedure:** FDA will notify the requester in writing of the date, time, and place for the meeting, as well as expected Center participants following receipt of a formal meeting request. Table 3 below indicates the timeframes for FDA's response to a meeting request.

[10] FDA will update the Guidance for Industry, *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*, to provide relevant examples of when an MDM may be appropriate. FDA will also include additional information in the guidance regarding what should be captured in the meeting request.

Table 3: Timelines for Responding to Meeting Requests

MEETING TYPE	RESPONSE TIME (CALENDAR DAYS)
A	14
B	21
B(EOP)	14
C	21
D	14
INTERACT	21

i. For any type of meeting, the sponsor may request a written response to its questions rather than a face-to-face[11] or teleconference meeting. FDA will review the request and make a determination on whether a written response is appropriate or whether a face-to-face or teleconference meeting is necessary. If a written response is deemed appropriate, FDA will notify the requester of the date it intends to send the written response in the Agency's response to the meeting request. This date will be consistent with the timeframes specified in Table 4 below for the specific meeting type.

ii. For pre-IND, Type C, Type D, and INTERACT meetings only, while the sponsor may request a face-to-face meeting, the Agency may determine that a written response to the sponsor's questions would be the most appropriate means for providing feedback and advice to the sponsor. Therefore, within these meeting types when a sponsor believes a face-to-face meeting is necessary for a particular meeting request, the sponsor should include a specific rationale with the initial meeting request explaining why the face-to-face format is warranted for the requested meeting. FDA will consider this justification with the meeting request, and if FDA determines a written response is sufficient, FDA will include a specific rationale (e.g., questions are purely clarifying, issues previously addressed in guidance or precedent, advice was previously provided on the same topic/question as part of a face-to-face meeting) for the decision in the communication notifying the sponsor of the date FDA intends to send the written response (consistent with timeframes specified in Table 4 below). For meeting requests within the above specified meeting types when a sponsor does not provide a rationale for a face-to-face meeting format, and FDA determines that the meeting request can be appropriately addressed through a written response, FDA will notify the requester of the date it intends to send the written response in the Agency's response to the meeting request. This date will be consistent with the timeframes specified in Table 4 below for the specific meeting type.

[11] A "face-to-face" meeting includes both in-person meetings and virtual meetings on IT platforms that allow for both audio and visual communication.

b. **Performance Goal:** FDA will respond to meeting requests and provide notification within the response times noted in Table 3 for 90% of each meeting type.

3. Scheduling Meetings

a. **Procedure:** FDA will schedule the meeting on the next available date at which all applicable Center personnel are available to attend, consistent with the component's other business; however, the meeting should be scheduled consistent with the type of meeting requested. Table 4 below indicates the timeframes for the scheduled meeting date following receipt of a formal meeting request, or in the case of a written response, the timeframes for the Agency to send the written response. If the requested date for any meeting type is greater than the specified timeframe, the meeting date should be within 14 calendar days of the requested date.

Table 4: Timelines for Scheduling Meetings or Sending Written Responses

MEETING TYPE	MEETING SCHEDULING OR WRITTEN RESPONSE TIME
A	30 calendar days from receipt of meeting request
B	60 calendar days from receipt of meeting request
B(EOP)	70 calendar days from receipt of meeting request
C	75 calendar days from receipt of meeting request
D	50 calendar days from receipt of meeting request
INTERACT	75 calendar days from receipt of meeting request

b. **Performance Goal:** Type A, B, B(EOP), C, D, and INTERACT meetings: 90% of meetings are held within the timeframe for each meeting type, and 90% of written responses are sent within the timeframe for each meeting type.

4. Meeting Background Packages

The timing of the Agency's receipt of the sponsor background package for each meeting type (including those meetings for which a written response will be provided) is specified in Table 5 below.

Table 5: Timelines for Agency Receipt of Background Packages

MEETING TYPE	RECEIPT OF BACKGROUND PACKAGE
A	At the time of the meeting request
B	30 calendar days before the date of the meeting or expected written response
B(EOP)	50 calendar days before the date of the meeting or expected written response*
C[12]	47 calendar days before the date of the meeting or expected written response*
D	At the time of the meeting request
INTERACT	At the time of the meeting request

***** If the scheduled date of a Type B(EOP) or C meeting is earlier than the timeframes specified in Table 4, the meeting background package will be due no sooner than 6 calendar days and 7 calendar days following the response time for Type B(EOP) and C meetings specified in Table 3, respectively.

5. Preliminary Responses to Sponsor Questions

a. **Procedure:** The Agency will send preliminary responses to the sponsor's questions contained in the background package no later than five calendar days before the meeting date for Type B(EOP), C, D, and INTERACT meetings. For all other meeting types, the FDA intends to send the requester its preliminary responses no later than 2 calendar days before the meeting.

b. **Performance Goal:** 90% of preliminary responses to questions for Type B(EOP), D, and INTERACT meetings are issued by FDA no later than five calendar days before the meeting date.

6. Sponsor Notification to FDA

Not later than three calendar days following the sponsor's receipt of FDA's preliminary responses for a Type B(EOP), C, D, or INTERACT meeting, the sponsor will notify FDA of whether the meeting is still needed, and if it is, the anticipated agenda of the meeting given the sponsor's review of the preliminary responses.

7. Meeting Minutes

a. **Procedure:** The Agency will prepare minutes that will be available to the sponsor 30 calendar days after the meeting for Type A, B, B(EOP), C, and D. The minutes will clearly outline the important agreements, disagreements, issues for further discussion, and action items from the meeting in bulleted form and need not be in great detail.

[12] For Type C meetings that are requested as early consultations on the use of a new surrogate endpoint to be used as the primary basis for product approval in a proposed context of use, the meeting background package is due at the time of the meeting request. Refer to section I.K.2 of this document.

Meeting minutes are not required if the Agency transmits a written response for any meeting type. For INTERACT meetings, preliminary responses will be annotated and resent within 30 calendar days if advice provided changes as a result of the meeting. In cases of a WRO, the WRO will serve as meeting minutes from FDA.

b. **Performance Goal:** 90% of minutes are issued within 30 calendar days of the date of the meeting.

8. Conditions

For a meeting to qualify for these performance goals:

a. A written request must be submitted to the review division.

b. The written request must provide:

i. A brief statement of the purpose of the meeting and the sponsor's proposal for either a face-to-face/virtual/teleconference meeting or a written response from the Agency;

ii. A listing of the specific objectives/outcomes the requester expects from the meeting;

iii. A proposed agenda, including estimated times needed for each agenda item;

iv. A listing of planned external attendees;

v. A listing of requested participants/disciplines representative(s) from the Center with an explanation for the request as appropriate; and

vi. The date that the meeting background package will be sent to the Center. Refer to Table 5 for timeframes for the Agency's receipt of background packages.

c. The Agency concurs that the meeting will serve a useful purpose (i.e., it is not premature or clearly unnecessary). However, requests for a Type B or B(EOP) meeting will be honored except in the most unusual circumstances.

9. Guidance, Clarity, and Transparency

a. By September 30, 2028, FDA will issue a revised draft of the existing guidance on "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products" with information pertaining to MDM requests and WRO procedures. In addition, FDA will update relevant MAPPs and SOPPs.

b. **Follow-Up Opportunity:** For all meeting types, to ensure the sponsor's understanding of FDA feedback from meeting discussions or a WRO, sponsors may submit clarifying questions to the Agency. Only questions of a clarifying nature will be permitted, i.e., to confirm something in minutes or a WRO issued by FDA, rather than raising new issues or new proposals. FDA may exercise discretion about whether requests are in-scope. The clarifying questions should be sent in writing as a "Request for Clarification" to the FDA within 20 calendar days following receipt of meeting

minutes or a WRO. For questions that meet the criteria, FDA will issue a response in writing within 20 calendar days of receipt of the clarifying questions. FDA's response will reference the original meeting minutes or WRO.

10. Assessment of Enhancements to Formal Meetings

Beginning in FY 2028, FDA will partner with a third party to assess the effectiveness of two enhancements introduced in PDUFA VIII: (1) requests for written responses and face-to-face meetings, described in section I.K.2.a.ii and (2) multi-divisional meetings, described in section I.K.1. The third party will have expertise in assessing the quality and efficiency of regulatory review programs.

For the requests for written responses and face-to-face meetings, FDA and the third party will catalog and analyze the number and type of requests received, the rationale for requesting the desired format, the Agency's response and timeframe for either scheduling or responding to the meeting request, and the timing of any responses to clarifying correspondence from sponsors. For the multi-division meetings, FDA and the third party will catalog and analyze the number of requests received, the rationale for requesting the meetings, the Agency's response and timeframe for accepting or denying the meeting request, and the timeframe for scheduling. For a sample of applications, FDA and the third party will also review communications and conduct interviews with sponsors and review teams to:

a. For WRO requests: Identify best practices for requesting and leveraging written responses;

b. For face-to-face rationales: Identify best practices for leveraging face-to-face (including video conference) and teleconference meetings, assess the clarity and consistency of FDA and sponsor rationales, and characterize reasons for conversion of face-to-face requests to WROs; and

c. For multi-divisional meetings: Identify best practices for leveraging multi-divisional meetings, including a characterization of the scope and type of questions asked, meeting types granted, the number of review divisions involved, and assessment of the benefits of multi-divisional meetings, in terms of promoting efficiency and alignment.

FDA and the third party will use the data to provide an assessment of the effectiveness of the enhancements and suggest actionable recommendations to help FDA and sponsors improve their communications.

Deliverables:

a. By March 31, 2030, FDA will publish an interim assessment report for public comment.

b. By March 31, 2032, FDA will publish a final report on its public website. This report will include findings from the assessment as well as recommendations for increasing the effectiveness of these enhancements.

L. EXPEDITING DRUG DEVELOPMENT AND ENHANCING THE USE OF REGULATORY SCIENCE TOOLS

Timely, interactive communications between FDA and sponsors during drug development is a core activity. The goal is to facilitate the conduct of efficient and effective drug development programs, which can enhance public health by making new safe and effective drugs available to the American public in a timely manner.[13] To ensure that new and innovative products are developed and available to patients in a timely manner, FDA will continue to ensure the sustained success of the breakthrough therapy program, continue early consultations between FDA and sponsors on the use of new surrogate endpoints as the primary basis for product approval, advance rare disease drug development, and advance the development of combination products. FDA will also continue to enhance the appropriate use of regulatory science tools to support drug development and regulatory review.

1. Ensuring Sustained Success of Breakthrough Therapy Program

Breakthrough therapy designation is intended to expedite the development and review of drug and biological products, alone or in combination, for serious or life-threatening diseases or conditions when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies.[14] A breakthrough therapy designation includes the features of the fast track program, intensive FDA guidance on an efficient drug development program, and an organizational commitment by FDA involving senior managers.[15] FDA will continue to retain current resources to enable the Agency to continue to work closely with sponsors throughout the breakthrough therapy designation, development, and review processes. Both FDA and the regulated industry are committed to ensuring the expedited development and review of innovative therapies for serious or life-threatening diseases or conditions by investing additional resources into the breakthrough therapy program.

2. Early Consultation on the Use of New Surrogate Endpoints

FDA and the regulated industry believe that early consultation between review teams and sponsors is important for development programs where the sponsor intends to use a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. Early consultation in the drug development program allows the review team to consult with FDA senior management to evaluate the sponsor's proposal before providing advice regarding the proposed biomarker as a new surrogate endpoint to support accelerated or traditional approval.

Requests to engage with FDA on this topic will be considered a Type C meeting request. The purpose of this meeting is to discuss the feasibility of the surrogate as a primary endpoint and identify any gaps in knowledge and how they might be addressed. The outcome of this

[13] FDA will update the guidance, Best Practices for Communication Between IND Sponsors and FDA During Drug Development, to reflect changes made in PDUFA VIII.
[14] See section 506(a) of the Federal Food, Drug, and Cosmetic (FD&C) Act, 21 U.S.C. § 356(a).
[15] See FDA Guidance for Industry entitled "Expedited Programs for Serious Conditions – Drugs and Biologics". A drug designated as a breakthrough therapy may also qualify for one or more of the other expedited programs as described in this guidance.

meeting may require further investigation by the sponsor and discussion and agreement with the Agency before the surrogate endpoint could be used as the primary basis for product approval. To qualify for this consultation, these Type C meeting requests must be accompanied by the complete meeting background package at the time the request is made that includes preliminary human data indicating impact of the drug on the biomarker at a dose that appears to be generally tolerable. The remaining meeting procedures as described in section I.K of this document will apply.

3. Advancing Development of Drugs for Rare Diseases

FDA will build on the success of rare disease programs in CDER and CBER by continuing to advance and facilitate the development and timely approval of drugs and biologics for rare diseases, including rare diseases in children. The Rare Diseases Team staff in CDER will continue to be integrated into review teams for rare disease development programs and application review to provide their unique expertise on flexible and feasible approaches to studying and reviewing such drugs to include, for example, innovative use of biomarkers, consideration of non-traditional clinical development programs, use of adaptive study designs, evaluation of novel endpoints, application of new approaches to statistical analysis, and appropriate use of FDA's expedited development and review programs (i.e., Fast Track, Breakthrough, Priority Review, and Accelerated Approval). CBER, through its Rare Disease Program Staff, will also ensure that its review offices consider such flexible and feasible approaches in review.

The rare disease staff will also continue to provide training to all CDER and CBER review staff related to development, review, and approval of drugs for rare diseases as part of the reviewer training core curriculum. The objective of the training will be to familiarize review staff with the challenges associated with rare disease applications and strategies to address these challenges; to promote best practices for review and regulation of rare disease applications; and to encourage flexibility and scientific judgment among reviewers in the review and regulation of rare disease drug development and application review. The training will also emphasize the important role of the rare disease staff as members of the core review team to help ensure consistency of scientific and regulatory approaches across applications and review teams.

Rare disease staff will continue to engage in outreach to the regulated industry, patient groups, and other stakeholders to provide training on FDA's rare disease programs. The staff will continue to foster collaborations in the development of tools (e.g., patient reported outcome measures) and data (e.g., natural history studies) to support development of drugs for rare diseases. In addition, the staff will also facilitate interactions between stakeholders and FDA review divisions to increase awareness of FDA regulatory programs and engagement of patients in FDA's regulatory decision-making.

FDA will convene Rare Disease Innovation, Science, and Exploration (RISE) workshops to facilitate scientific exchange, identify challenges, and promote solutions that support efficient and effective development and review of therapies for rare diseases. The workshops will focus primarily where significant development challenges exist, with the goal of addressing key scientific and drug development barriers and informing regulatory decision making across CDER and CBER. FDA will convene up to 10 RISE workshops, at least one annually,

from FY 2028-2032. FDA will publicly solicit topics for RISE Workshops, and the Workshops themselves will incorporate engagement from the regulated industry, academia, and patient advocates. After each RISE workshop, a publicly available summary will be prepared that includes recommended action items. FDA will use insights from the workshops to inform rare disease review work, such as in the development of guidance documents and reviewer training, as appropriate.

FDA will include updates on the activities and success of the rare disease programs in the PDUFA annual performance report to include, for example, the number of training courses offered and staff trained, the number of review programs where rare disease staff participated as core team members, and metrics related to engagement with external stakeholders. FDA will also continue to include information on rare disease approvals in its annual reports on innovative drug approvals, including utilization of expedited programs and regulatory flexibility and appropriate comparative metrics to non-rare disease innovative approvals.

a. **Rare Disease Endpoint Advancement (RDEA) Program**

The lack of regulatory precedent, small trial populations, and/or limited understanding of disease natural history associated with rare diseases creates unique challenges when determining the appropriate efficacy endpoint(s) for clinical trials intended to evaluate the effectiveness of rare disease therapies. Though difficult to establish, well-developed efficacy endpoints, especially those that could apply to other rare diseases with similar manifestations, drive the general advancement of rare disease drug development. In addition to challenges associated with developing endpoints that appropriately capture key signs and symptoms of a rare disease and directly measure how patients feel, function, or survive, surrogate endpoint development is also challenging in diseases with slow progression, small patient populations, or other challenges commonly associated with drug development in rare diseases.

Prior to implementation of the Rare Disease Endpoint Advancement (RDEA) Pilot program in PDUFA VII, mechanisms for sponsors of rare disease drug development programs to collaborate with FDA were not structured to provide repeated, intensive interactions with the Agency. To support the advancement of rare disease treatments, FDA established the RDEA pilot program in PDUFA VII. FDA will continue to build on the success of the RDEA Pilot Program, providing a mechanism for supporting efficacy endpoint development for drugs that treat rare diseases by offering additional engagement opportunities with the Agency to sponsors of development programs that meet specific criteria. FDA will publish a Federal Register Notice no later than the end of the first quarter of FY 2028 announcing the continuation of the RDEA program. In addition, FDA will continue to develop the staff capacity to enable and facilitate appropriate development and use of these types of novel endpoints. This staff will support the complex and intensive review work necessary to evaluate novel endpoint development with a focus on the challenges of trial designs utilizing small populations.

i. **Scope:** The RDEA program will seek to advance rare disease drug development programs by providing a mechanism for sponsors to collaborate with FDA throughout the efficacy endpoint development process. An endpoint, or endpoints, will be considered eligible for RDEA if each of the following criteria are met:

1) The associated development program should be active and address a rare disease, with an active IND or pre-IND for the rare disease.

    a) Sponsors who do not yet have an active development program but have, or are initiating, a natural history study where the proposed endpoint is intended to be studied are also eligible to apply.

    b) The FDA may also consider accepting a proposal for a development program for a common disease that includes innovative or novel endpoint elements, including the specific endpoint and/or the methodology being developed, if there is sufficient justification that the proposal could be applicable to a rare disease.

2) The proposed endpoint is a novel efficacy endpoint intended to establish substantial evidence of effectiveness for a rare disease treatment.

    a) An endpoint is considered novel if it has never been used to support drug approval or if it has been substantially modified from previous use to support drug approval.

    b) Preference will be given to proposals that have the potential to impact drug development more broadly, such as one that uses a novel approach to develop an efficacy endpoint or an endpoint that could potentially be relevant to other diseases. Preference will also be given to accepting proposals that reflect a range of different types of endpoints.

    c) For surrogate endpoint proposals, preference will be given to those with novel approaches for collecting additional clinical data in the pre-market stage to advance the validation of these endpoints. If the sponsor is proposing to develop a surrogate endpoint as part of a rare disease application, participation in a prior Type C Surrogate Endpoint meeting is encouraged.

ii. **Overview of Process and Timeline:** FDA will utilize a phased implementation to transition the RDEA pilot program to the established meeting framework. From FY 2028-2029, the RDEA pilot program will continue, and sponsors should submit proposals for potential participation. From FY 2030-2032, the RDEA pilot program will transition to Type C-RDEA meetings.[16]

1) From FY 2028-2029, FDA will select a limited number of qualified proposals for admission into RDEA:

    a) FY 2028: FDA will accept a maximum of 4 proposals.

    b) FY 2029: FDA will accept a maximum of 6 proposals.

2) From FY 2030-2032, the RDEA pilot program will transition to Type C-RDEA meetings under the formal PDUFA meetings paradigm.

[16] This designation is not intended to suggest a new meeting type. It is a Type C meeting focused on RDEA.

iii. **Process for FY 2028-2029:** The following steps summarize the process for applying to and participating in the RDEA pilot program:

1) A sponsor who believes a development program qualifies for participation in RDEA will submit a proposal to FDA that includes a justification addressing each of the criteria described above, including scientific justification for why the endpoint is being explored to measure meaningful clinical benefit in the disease/condition and, relevant summaries of pertinent information related to the endpoint from prior studies.

2) FDA will confirm receipt of the sponsor's proposal within 14 days of receipt.

3) FDA will notify the sponsor with a final selection decision no later than 60 days following the end of the FY quarter during which it is submitted.

4) Sponsors admitted to the RDEA pilot may participate in up to 2 focused meetings with relevant FDA staff to discuss endpoint development.

    a) The sponsor will provide a briefing document upon submission of each meeting request.

    b) Each meeting will be scheduled within 60 days following FDA's receipt of the sponsor's meeting request and complete briefing document.

    c) The scheduling timeline may be shortened for meeting requests to discuss narrow issues and/or questions at FDA's discretion.

    d) The timing between each meeting is flexible and depends on how much time the sponsor needs to identify new issues and/or questions and prepare required materials for the next meeting.

    e) RDEA meeting requests should be submitted no later than 2 years from the date of admittance into the RDEA Pilot Program.

5) Sponsors who have completed the maximum of 2 RDEA meetings or do not have additional endpoint-focused questions or issues to discuss with FDA may proceed with the standard regulatory submission process.

    a) FDA's advice provided during and between RDEA meetings does not constitute a regulatory decision and is considered non-binding. Completing the 2 RDEA meetings does not guarantee approval for a regulatory submission that includes efficacy endpoints discussed during RDEA meetings.

    b) After completion of 2 RDEA meetings, the sponsor can request additional input from FDA, as needed, through other formal meeting mechanisms, such as Type B, Type C, Type C Surrogate Endpoint, or Type D meetings.

6) Sponsors who do not participate in the pilot will have an opportunity to interact with the Agency through traditional channels.

iv. **Process and Timeline (FY 2030-2032):** From FY 2030-2032, requests to engage with FDA on this topic will be considered a Type C meeting request under the formal PDUFA meetings paradigm. The purpose of this meeting is to discuss novel efficacy endpoint development for drugs that treat rare diseases with sponsors of development programs that meet specific criteria.

To qualify for a Type C-RDEA meeting, the request must fall within the scope and criteria outlined in 1a, 1b, and 2a of this section. Type C-RDEA meetings will follow established Type C meeting timelines.

v. **Transparency and Endpoint Advancement:** As part of RDEA, FDA will conduct up to 3 public workshops by the end of FY 2032 to discuss various topics relevant to endpoint development for rare diseases. To promote innovation and evolving science, novel endpoints developed through RDEA may be presented by FDA, such as in guidance documents, on a public-facing website, or at public workshops as case studies.

4. Advancing Development of Drug-Device and Biologic-Device Combination Products Regulated by CBER and CDER

a. **For Use-Related Risk Analysis (URRA)**

Sponsors employ URRA to identify the need for risk mitigation strategies and to design a human factors (HF) validation study. Based on a URRA, a sponsor may propose that a HF validation study is not needed to be submitted to support the safe and effective use of a drug-device or biologic-device combination product. FDA will establish the following procedures for review of URRAs for combination products:

i. The sponsor should submit a request for review of their URRA to their IND. The submission should include specific questions, justification that a HF validation study is not needed to be submitted including any supporting information, and scientific and regulatory requirements for which the sponsor seeks agreement.

ii. Within 60 days of Agency receipt of the URRA and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the URRA and answers to the questions posed by the sponsor. If the Agency does not agree that either the URRA or the sponsor's justification are adequate to support the absence of a HF validation study, the reasons for the disagreement will be explained in the response.

iii. URRA submission performance goal: FDA will review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.

iv. Sponsors may still elect to submit a URRA with a HF validation protocol and will only be subject to timelines in section I.L.4.b, For Human Factors Validation Study Protocols.

b. **For Human Factors Validation Study Protocols**

Human factors studies are conducted to evaluate the user interface of a drug-device or biologic-device combination product to eliminate or mitigate use-related hazards that may affect the safe and effective use of the combination product.

Over the past decade, more combination products have been developed to deliver therapeutics via different routes of administration (e.g., parenteral, inhalation) with complex engineering designs. HF validation protocols are reviewed during the IND stage with the goal towards developing a final finished combination product that supports the marketing application. To achieve this objective, FDA will establish the following procedures for review of HF validation study protocols:

i. The sponsor should submit a human factors protocol to the IND with specific questions, including scientific and regulatory requirements for which the sponsor seeks agreement (e.g., are the study participant groups appropriate to represent intended users, is the study endpoint adequate, are the critical tasks that should be evaluated appropriately identified).

ii. Within 60 days of Agency receipt of the protocol and specific questions, the Agency will provide a written response to the sponsor that includes a succinct assessment of the protocol and answers to the questions posed by the sponsor. If the Agency does not agree that the protocol design, execution plans, and data analyses are adequate to achieve the goals of the sponsor, the reasons for the disagreement will be explained in the response.

Performance goals for FDA will be as follows:

iii. Review and provide sponsor with written comments for 90% of human factors validation protocol submissions within 60 days of receipt of protocol submission.

5. Regulatory Science Tools to Support Drug Development and Regulatory Review

Delivering new medicines to patients through biomedical innovation requires advances in regulatory science tools to support drug development and regulatory review. FDA will integrate into review practice the lessons learned from its efforts on benefit-risk assessment in regulatory decision-making, complex innovative designs, digital health technologies, the drug development tools qualification pathway for biomarkers, model-informed drug development, patient-focused drug development, and real-world evidence.

a. **Benefit-Risk Assessment in Regulatory Decision-Making**

Benefit-risk assessment is a foundation of FDA's regulatory review of marketing applications for new human drugs and biologics. The Benefit-Risk Framework is described in the Benefit-Risk Assessment for New Drug and Biological Products

Guidance for Industry.[17] FDA currently includes the Benefit-Risk Framework in its NDA and BLA review training, processes, and templates to support the conduct and communication of its benefit-risk assessment.

FDA is committed to continuing its implementation and application of structured benefit-risk assessment in its regulatory review processes and documentation. FDA will continue to explore additional opportunities to enhance its use and communication of its benefit-risk assessments for new drug and biological review.

b. **Complex Innovative Designs**

The Complex Innovative Design program will be incorporated into standard review practice. FDA will continue to maintain staff capability and capacity to facilitate the advancement and use of complex adaptive, Bayesian, and other novel clinical trial designs. FDA will ensure there are appropriate Subject Matter Experts (SMEs) and oversight for the review of complex innovative designs. Sponsors may seek advice on the design and analysis of complex innovative studies through traditional formal meeting requests (e.g., type C meetings) or as part of a special protocol assessment of an eligible protocol. Sponsors may request participation by relevant FDA SMEs in such meetings.

c. **Digital Health Technologies**

FDA continues to recognize the capability of digital health technologies (DHTs), including those that are enabled by artificial intelligence (AI) to provide scientific and practical advantages in supporting the assessment of patients by generating information outside of the traditional clinic visit that could modernize drug development and support drug evaluation. Accordingly, in PDUFA VIII, FDA will continue to maintain PDUFA resources to support a consistent approach to the review of DHTs and to consider cross-center topics across FDA as appropriate, including by working with FDA's Digital Health Center of Excellence.

As advances are made in sensors and digital technology, and as the scope and utility of DHTs within drug development expands, FDA will be responsive to outside needs focusing on workshops, demonstration projects and guidances as applicable. Experiences gained through DHT demonstration projects and public meetings funded in PDUFA VII and in CDER and CBER's review of submissions incorporating DHTs will continue to support FDA's efforts to promote shared learning and consistency regarding DHT-based policy, procedure, and tool development and to incorporate such learnings into regulatory decision making.

d. **Drug Development Tools Qualification Pathway for Biomarkers**

To facilitate the continued use of the drug development tools qualification pathway for biomarkers, FDA will utilize staff capacity to facilitate biomarker qualification review. FDA will also continue to publish information on its website regarding biomarker

[17] Benefit-Risk Assessment for New Drug and Biological Products Guidance for Industry: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/benefit-risk-assessment-new-drug-and-biological-products

qualification submissions under section 507 of the FD&C Act, consistent with the requirements in section 507(c), and to update the website quarterly.

Sponsors who do not use this qualification pathway will have an opportunity to interact with the Agency through traditional channels.

e. **Model-Informed Drug Development**

FDA will build on the successes and demonstrated impact of the Model-Informed Drug Development (MIDD) Paired Meeting Program by further developing staff capacity and implementing operational enhancements designed to increase access to the MIDD meeting program. By no later than the end of the 1st quarter of FY 2028, FDA will publish a Federal Register Notice announcing the continuation of the MIDD meeting program and outline any updates to the process, scope of relevant meeting topics, and submission and response timelines.

FDA will use a phased implementation strategy to meet increases in the volume of MIDD meeting requests. Starting in FY 2028, FDA will increase the number of eligible proposals accepted on a quarterly basis.

After FY 2028, FDA will further increase access to the MIDD meeting program in a phased manner with eventual transition to a Type C - MIDD meeting[18] such that sponsors may request a Type C - MIDD meeting at any point during drug development. FDA will work towards eliminating the quarterly cadence and cap on the number of meeting requests by the end of FY 2030. Type C - MIDD meeting requests will be considered on a rolling basis in real time and follow established Type C meeting timelines.

To maximize flexibility and opportunities for continuous regulatory engagement, sponsors participating in the Type C - MIDD meetings will be granted one meeting per request. These meetings will be led by the relevant MIDD/quantitative medicine leadership in partnership with clinical/medical, biostatistics, and other relevant discipline staff and leadership to ensure alignment with decision makers.

FDA will continue to facilitate the advancement and use of emerging MIDD approaches and their integration into practice through the efforts of the Quantitative Medicine Center of Excellence.

f. **Patient-Focused Drug Development**

Patient-focused drug development (PFDD) is a systematic approach to collect and utilize robust and meaningful patient and caregiver experiences, perspectives, needs, and priorities that can inform drug development and regulatory decision-making.

FDA is committed to continuing its PFDD program to advance the collection and use of patient experience data to inform drug development. FDA will continue to raise awareness about how patient experience data should be submitted to an NDA or BLA to facilitate FDA review and to be considered in regulatory decision-making, including labeling, as appropriate.

[18] This designation is not intended to suggest a new meeting type. It is a Type C meeting focused on MIDD.

To ensure shared learnings from use of patient experience data across drug development programs and review divisions, FDA intends to:

i. Publish case studies at least two times by the end of FY 2032 demonstrating how patient experience data was considered in specific regulatory decisions across different therapeutic areas, highlighting when patient experience data was used and when it was not used to inform regulatory decision-making.

ii. By the end of FY 2030, host a public meeting to discuss case studies and facilitate broader dialogue about the collection, submission, and use of patient experience data in drug development and regulatory review. FDA's goal is to publish the FDA case studies that will be presented at the meeting at least 21 days in advance of the meeting date.

iii. Continue to conduct internal and external trainings and outreach focused on improving understanding of patient-focused methods, common methodological challenges observed during regulatory review, and considerations relevant to the incorporation of patient-focused methods in drug development programs and regulatory decision-making, including labeling.

FDA will continue to make public a brief statement in the review document regarding the patient experience data and related information, if any, submitted and reviewed as part of an application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act.

g. **Real-World Evidence**

FDA recognizes the significant value of real-world data (RWD) and real-world evidence (RWE) in supporting regulatory decision-making throughout the product lifecycle. In accordance with section 3022 of the 21st Century Cures Act, FDA remains dedicated to advancing the use of RWE to support new intended labeling claims, including the approval of new indications, populations, or dosing information, or to support or satisfy post-approval study requirements. FDA's commitment to advancing real-world evidence reflects the shared goal of bringing safe and effective treatments to patients while maintaining rigorous scientific standards for regulatory decision-making.

Review of RWE related submissions will continue via established review practice and FDA will maintain dedicated PDUFA resources to support RWD/ RWE initiatives and continue to train relevant subject matter experts (SMEs) and review team members in RWE-related methodologies to facilitate consistent evaluation of RWE submissions. FDA will engage with sponsors on the appropriateness and acceptability of submissions through formal meeting requests, and sponsors may request participation by relevant FDA SMEs in such meetings.

Experiences gained in CDER and CBER will be used to periodically update existing RWE-related guidance documents or generate new draft guidance, as appropriate.

FDA will continue to report aggregate and anonymized information, on at least an annual basis and based on available sources (e.g., information provided by review divisions), describing RWE submissions to CDER and CBER. The reports will describe application

type (e.g., primary focus on safety or effectiveness), data sources used (e.g., medical claims, electronic health records, registries, digital health technologies), study design employed (e.g., randomized trial, externally controlled trial, observational study), and regulatory request (e.g., new indication, population, dosing information, post-approval study requirement for a marketed product). FDA, as appropriate, will summarize the characteristics of RWD/RWE that contributed to the determination of substantial evidence of effectiveness for each new indication approval and will link to relevant published review documents when citing specific NDA/BLA approvals.

6. Reviewer Training on Regulatory Science Tools

FDA will conduct ongoing reviewer training for all relevant staff and update relevant MAPPs and SOPPs, as appropriate, to ensure that staff have a working knowledge of available regulatory science tools addressed in section L.5 of this letter. The objectives of this training will be to familiarize review staff with the available tools, to promote best practices, and to encourage appropriate use among reviewers when evaluating drug development proposals and applications containing these tools. The training will also help promote consistency of scientific and regulatory approaches across applications and review teams.

7. Communicating the Use of Regulatory Science Tools

Over several decades, different regulatory science tools to facilitate drug development and regulatory decision-making have been developed as part of and external to the PDUFA programs. Increasing transparency and communication on how these regulatory science tools have been applied across different drug development contexts to promote shared learning across multiple stakeholders will advance the application of these approaches in drug development and their use in regulatory decision-making.

By the end of FY 2028, FDA will hold a public meeting to discuss best practices for communicating the use of regulatory science tools in drug development and regulatory decision-making. As regulatory science tools (e.g., complex innovative trial design, model-informed drug development, real-world evidence) are used across drug development programs and evaluated by regulatory review teams, it is important for all relevant stakeholders to understand the benefits and limitations of these approaches in specific drug development contexts. The meeting will solicit stakeholder input on how the regulated industry, FDA, and the stakeholder community can enhance public communication regarding the use of regulatory science tools in regulatory decisions while preserving scientific flexibility and avoiding unnecessary administrative burden. The workshop will focus on what information may be most useful for different audiences and what communication methods would be most effective.

Within 6 months of the public meeting, FDA will issue a summary report of the meeting that will include potentially actionable recommendations to the regulated industry and FDA on communication approaches to increase transparency and shared learnings across multiple stakeholders.

8. Enhancing Bioinformatics Support

To facilitate submission and review of bioinformatics and computational biology information, FDA will continue to leverage expertise and staff capacity in support of the human drug review program to efficiently review and provide technical and timely feedback on information and accompanying data in submissions and meet PDUFA performance goals. FDA will maintain staff with specialized expertise in specific product/therapeutic areas to facilitate translation of bioinformatic information to subject matter review experts.

FDA will continue to provide appropriate data and technology modernization resources related to bioinformatics to support the human drug review program and to ensure meeting PDUFA performance goals. FDA will continue to assess its bioinformatics capabilities, and, annually, ensure that IT resources are provided to support bioinformatics activities, including software licensing, cloud-based storage and computing capacity, operations support and maintenance. FDA will continue to advance harmonization of the bioinformatic data standards and methodologies globally. Outcomes to enhance bioinformatics support will be shared at regularly scheduled FDA-industry meetings.

M. ENHANCEMENT AND MODERNIZATION OF THE FDA DRUG SAFETY SYSTEM

FDA will continue to use user fees to enhance the drug safety system, including adopting new scientific approaches, improving the utility of existing tools for the detection, evaluation, prevention, and mitigation of adverse events, modernizing REMS assessments, and coordinating regulatory activity in the pre-market and post-market settings. Enhancements to the drug safety system will improve public health by increasing patient protection while continuing to enable access to needed medical products.

User fees will provide support for 1) modernization and improvement of REMS assessments and 2) maintenance of Sentinel Initiative capabilities and continued integration into FDA drug safety activities.

1. Modernization and Improvement of REMS Assessments

FDA will use user fee funds to help support the aim of modernizing and improving REMS assessments by incorporating REMS assessment planning into the design of REMS and help support the aim of increasing the efficiency of FDA's review of REMS assessment reports. FDA will continue performance goals for review of REMS assessment methods and study protocols.

a. FDA will review and notify sponsor with concurrence or comments within 90 days of receipt for 90% of REMS assessment methods and protocols.

2. Optimization of the Sentinel Initiative

FDA and the regulated industry have the shared goal of continuing to enhance the Sentinel system to promote the efficiency and effectiveness of Sentinel's ability to contribute to regulatory decision-making. FDA will use user fee funds to maintain the high-quality and large quantity of data available to support the Agency's pharmacoepidemiology needs,

advance implementation of the Sentinel 3.0 operating model through support for data infrastructure, and sustain the processes and tools required to ensure appropriate use of these data, including comprehensive training of review staff. To enhance communication prior to product approval about the approach to a possible postmarketing requirement (PMR) for non-interventional studies, FDA intends to explore the potential for establishing a process under which sponsors may voluntarily submit a concept brief describing the sponsor's proposed approach to evaluating a safety issue that could potentially be the subject of a PMR under Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act.

These efforts will help enable FDA to address product-safety regulatory questions, to support the aim of increasing Active Risk Identification and Analysis (ARIA) sufficiency, and to advance the use of real-world evidence in evaluating drug and biologic safety and effectiveness. To that end, FDA commits to:

a. Streamlined Annual Reporting: Simplified reporting of metrics describing the use of Sentinel for regulatory purposes.

b. Biannual Updates on Sentinel: FDA will jointly plan and conduct meetings with the regulated industry on the plans and progress for Sentinel 3.0.

N. ADVANCING CHEMISTRY, MANUFACTURING, AND CONTROLS (CMC) FACILITY ASSESSMENT: A RISK-BASED LIFECYCLE APPROACH

To support the timely development and availability of new and innovative products, FDA and the regulated industry will focus on enhancing Chemistry, Manufacturing, and Controls (CMC) communications during drug development and application review. FDA will continue to utilize user fees to support the use of alternate tools to assess manufacturing facilities in support of pending applications, four-part harmony in quality related communications, implementation of actions described in *FDA's Strategy Document on Innovative Manufacturing Technologies*, and training on processes and best practices for assessing CMC elements of an application. Experiences gained through commitments completed in PDUFA VII will continue to support FDA's efforts in enhancing communication during development and application review.

Manufacturing facility deficiencies observed on inspection could lead to complete response actions and the need for multiple review cycles. FDA and the regulated industry recognize a need to prevent or mitigate such deficiencies by fostering earlier and more transparent communication on CMC facility topics that could lead to their early resolution. FDA and the regulated industry recognize that additional opportunities for engagement facilitate transparency, earlier shared understanding of regulatory requirements and expectations for manufacturing facilities, and proactive readiness for facility evaluation and inspection in support of drug applications. FDA and the regulated industry believe that this communication and engagement will provide a more proactive approach to timely address manufacturing facilities deficiencies, which could lead to an increase in first cycle approvals and facilitate the American public's timely access to safe, effective, and high-quality new drugs and biologics.

This PDUFA VIII CMC facility lifecycle program is designed to facilitate meeting this objective through new and enhanced engagement mechanisms between FDA and the regulated industry that may happen before, during, and after an application review cycle. Effective use of these

engagements aims to decouple or mitigate the occurrence of deficiencies that if unaddressed may lead to multiple review cycles.

1. Readiness For Pre-Approval Inspection (PAI) or Pre-License Inspection (PLI)

To provide greater transparency on FDA's requirements and expectations and support regulated industry readiness for facility evaluation and inspection supporting an NDA or BLA, including supplements, FDA will publish guidance, described in section N.8 below, describing the manufacturing facility readiness attributes that should be met, prior to facility evaluation and inspection. The guidance will describe how the regulated industry can use this information to self-assess facility readiness to reduce the probability of deficiencies that often cannot be corrected during the review cycle, and to ensure meaningful and timely manufacturing facility evaluation and inspections. The readiness criteria set forth in the guidance may also facilitate eligibility for post-PAI or post-PLI meetings, when warranted.

2. CMC Facility Pre-submission Meeting for an NDA or BLA, Including CMC Supplements Related to Manufacturing Facilities

Applicants may request a single CMC Facility Pre-submission meeting to discuss manufacturing facilities for a proposed application submission. Transparent sharing and discussion of this information can facilitate applicant and facility readiness, as well as FDA's assessment of the application with respect to facility evaluation and inspection. Such meetings shall include FDA representatives from relevant functions and are generally expected to occur 3-6 months before an application submission, though they may occur earlier or later.

Topics for this meeting may include, but are not limited to, information regarding manufacturing supply chain with focus on the relationships and interdependence of manufacturing facilities and the operations intended for the application product, awareness and mitigation of associated risks, and learnings from prior inspections conducted by FDA and other regulators. FDA's advanced awareness and assessment of other relevant quality information about the facilities and their operations will inform FDA's risk-based approach in making decisions for facility evaluations and inspections. The proposed topics should not focus on content suited for other existing meeting types or other engagement (e.g., Pre-Operational Review, CMC Type C, Type D).

3. Enhancing Inspection Communication for Applicants, Not Including Supplements

FDA and the regulated industry believe enhanced communication between review teams and the regulated industry on certain pre-license inspections and pre-approval inspections can facilitate an efficient application review process.

When FDA determines for an application, not including supplements, that it is necessary to conduct the inspection at a time when the product identified in the application is being manufactured, FDA's goal is to communicate its intent to inspect a manufacturing facility at least 60 days in advance of BLA Pre-license Inspections and NDA Pre-approval Inspections and no later than mid-cycle. FDA reserves the right to conduct manufacturing facility

inspections at any time during the review cycle, whether or not FDA has communicated to the facility the intent to inspect.

4. Post-PAI or Post-PLI Meeting for Original NDAs or BLAs, Not Including Supplements

The intent of the post-PAI or post-PLI meeting is to ensure transparency and enable resolution where possible of any outstanding deficiencies by the original action date. After FDA completes a PAI or PLI for an NDA or BLA and reviews findings, FDA intends to inform the applicant when observations communicated to a facility on the Form FDA 483 may result in a complete response action. Upon such notification, an applicant may request a meeting to discuss inspection findings that impact application approval and corrective actions to those findings, with the goal of facilitating transparency on whether corrective actions are responsive to the issues identified that may impact application approvability. FDA reserves the right to defer comment on acceptability of the corrective actions and approvability of the application but will strive to provide specific and actionable feedback. FDA shall include representatives from relevant functions in the post-PAI or Post-PLI meeting. When FDA grants a Post-PAI or Post-PLI meeting, FDA will strive to complete the meeting to facilitate first cycle approval by the originally assigned PDUFA Action Date, but may extend the goal date per section I.A.5. of the commitment letter.

5. Post-Action Meetings, Including CMC Supplements related to Manufacturing Facilities

When FDA issues a complete response letter for an NDA or BLA, including CMC supplements, due to deficiencies observed on a PAI or PLI, an applicant may request a Type A post-action meeting (outlined in section I.K: Meeting Management Goals) to discuss and gain understanding of those deficiencies that should be corrected before the application can be approved.

6. Meeting Procedures

a. Regarding **post-PAI and post-PLI meeting requests**, FDA intends for timelines and procedures to take application specific circumstances (e.g., priority goal dates, inspections that occur later in the review cycle), into consideration to facilitate meaningful discussion within the review cycle with the goal of implementing corrective actions that facilitate application approval.

b. **Meeting Requests**: The format and content of meeting requests should adhere to the recommendations outlined in the guidance "Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products."

c. **Responses to Meeting Requests**: FDA will notify the requester in writing of the date, time, and place for the meeting, as well as expected Center participants following receipt of a meeting request. FDA will strive to meet the timeframes listed below for responding to meeting request.

Table 6: Timelines for Responding to Facility Lifecycle Meeting Requests

MEETING TYPE	RESPONSE TIME (CALENDAR DAYS)
CMC Facility Pre-submission	21
Post-PAI/PLI	14
Post-Action	14

d. **Scheduling the Meeting Requests**: The meeting should be scheduled consistent with the type of meeting requested. FDA will strive to schedule the meeting within the timeframes listed below.

Table 7: Timelines for Scheduling Facility Lifecycle Meetings

MEETING TYPE	MEETING SCHEDULING (CALENDAR DAYS FROM MEETING REQUEST)
CMC Facility Pre-submission	60
Post-PAI/PLI	30
Post-Action	30

e. **Meeting Background Packages**: The timing of the Agency's receipt of the sponsor background package for each meeting type is specified in Table 8 below.

Table 8: Timelines for Agency Receipt of Facility Lifecycle Meeting Background Packages

MEETING TYPE	RECEIPT OF BACKGROUND PACKAGE
CMC Facility Pre-submission	30 calendar days before the date of the meeting
Post-PAI/PLI	At the time of the request
Post-Action	At the time of the request

f. **Preliminary Responses to Questions**: The Agency will send preliminary responses to the applicant's questions 2-5 calendar days prior to the meeting.

g. **Sponsor Notification to FDA**: Prior to the date of the meeting, the applicant will notify FDA of whether the meeting is still needed, and if it is, provide the anticipated agenda at least 1 business day in advance of the meeting.

h. **Meeting Minutes**: The Agency will prepare minutes that will be available to the applicant not later than 30 calendar days after the meeting. The minutes will clearly outline the important agreements, disagreements, issues for further discussion, and action items from the meeting. Meeting minutes need not be provided if the Agency transmits a written response for any meeting type.

7. CMC Facility Lifecycle Workshop and Third-Party Assessment

FDA will contract with an independent third party to conduct a public workshop which will be held no later than September 30, 2030. The public workshop will focus on program implementation and its impact on facility readiness and reduction of facility deficiencies. The topics for the workshop will be informed by the third-party assessment and include, but are not limited to, impact on the goals of inspection readiness and reduction in facility deficiencies, program operations (e.g., rate of meetings granted or denied, denial reasons, timing of meetings relative to significant milestones) and feedback from both FDA and the regulated industry on learnings to date. A third party will separately engage both FDA staff and individual sponsors through contractor-led interviews to assess the effectiveness of the facility lifecycle program. This third party will also assess the impact of the facility lifecycle program on facility-issue driven complete responses.

Following the close of the public comment period for the public workshop, the third-party that conducted the assessment described above will assess feedback from the workshop and draft a report summarizing the findings from the workshop, its assessment, and engagement with FDA and individual sponsors and identify best practices and areas for improvement for the regulated industry and FDA to enhance the CMC facility lifecycle program. The next steps may include proposed timeframes to develop or revise, as appropriate, relevant MAPPs or SOPPs and other applicable documents to incorporate lessons learned. FDA will publish the final report on the FDA's website no later than 9 months after the close of the comment period following the public workshop.

8. Guidance for Industry

By October 1, 2028, FDA will strive to publish draft guidance describing the implementation of this CMC facility lifecycle program. Such guidance will convey topics including, but not limited to, attributes that describe readiness for a PAI or PLI (as described in section N.1), CMC Facility Pre-submission, Post-PAI and Post-PLI, and Post Action meeting procedures, timelines, meeting type designation, criteria that FDA will consider when determining eligibility for each meeting (e.g., compliance classification, readiness for PAI/PLI criteria, meeting package completeness), best practices when submitting meeting request packages, and considerations regarding goal date extensions. FDA will strive to finalize the guidance within 24 months following close of the comment period.

O. ADVANCING THE DEVELOPMENT, REVIEW, AND APPROVAL OF NEXT GENERATION CELL AND GENE THERAPY PRODUCTS

FDA will build on the success of the Cell and Gene Therapy Program (CGTP) to ensure that the next generation of cell and gene therapy products are developed and made available to patients in a timely manner. The Agency will retain and further strengthen its staff capacity and capability to create predictability, speed development, and meet the challenges and demands of this rapidly advancing field.

CBER will utilize existing resources to sustain CGTP staff for direct review activities and other supportive activities (e.g., policy development, staff training, external outreach, stakeholder education/webinars, post-market safety), with a focus on hiring staff with technical, scientific,

clinical, and other specialized expertise necessary to facilitate the development and advancement of cell and gene therapies. CBER will continue to organize and manage the CGTP for optimal performance, including leveraging and implementing best practices.

CGTP will continue to maintain a highly trained and experienced staff, with an emphasis on remaining current in regulatory science and scientific, technical, manufacturing, and clinical advances. The CGTP staff training program will be reviewed and modified as needed to enhance the training of the program staff to maintain their competency. Among other topics, training will incorporate lessons learned from implementation of PDUFA VII initiatives supporting development of cell and gene therapies, prior workshops, listening sessions, and approaches to review reflected in published guidance.

The CGTP staff will continue to engage in outreach and solicit views from the regulated industry, patient groups, and other stakeholders on specific topics and proposals. Staff will participate in external collaborations, including public-private partnerships, fostering appropriate harmonization and development of tools (e.g., consensus standards), technologies, and approaches that support the development of cell and gene therapies. Interactions and external collaborations will also focus on advancing manufacturing and testing, such as development and implementation of emerging technologies, bioinformatics, and artificial intelligence/machine learning. CBER will continue to issue new guidance and/or update existing guidances (and relevant SOPPs), as appropriate, to remain current with evolving science and new approaches.

With stakeholders, CBER staff will continue discussing the use of existing approaches (e.g., surrogate endpoints, real-world evidence, complex innovative designs, natural histories) and explore new approaches for obtaining efficacy and safety information and expediting development with specific consideration and attention to rare diseases. In particular, CBER will continue to advance approaches to evaluate efficacy in small patient populations, as appropriate, using methods such as novel trial designs and statistical methods, as well as methods and approaches for capturing post-approval safety and efficacy data for cell and gene therapy products, as outlined in published guidance. CBER will also advance sponsors leveraging their prior knowledge (or other information for which the sponsor has a right of reference) and public knowledge consistent with applicable law, including Chemistry, Manufacturing, and Controls, non-clinical, and clinical knowledge, across therapeutic contexts in order to facilitate product development and application review.

FDA will continue to work with stakeholders to seek public input, as appropriate, on questions and challenges faced by cell and gene therapy developers, including the use of novel endpoints and the role of less defined natural histories to facilitate the development and approval of cell and gene therapies.

P. SUPPORTING REVIEW OF ALLERGENIC EXTRACT PRODUCTS

FDA will use fee revenues to support the review of allergenic extract products included in the PDUFA program. Allergenic extract products licensed after October 1, 2022 will generally be included in user fees. All performance goals, procedures, and commitments in this letter apply to the allergenic extract products included in the PDUFA program.

Allergenic extract products licensed before October 1, 2022, and standardized allergenic extract products submitted pursuant to a notification to the applicant from the Secretary regarding the

existence of a potency test that measures the allergenic activity of an allergenic extract product licensed by the applicant before October 1, 2022, are excluded from PDUFA. Epicutaneous-test diagnostic products are also excluded beginning in PDUFA VIII.

II. CONTINUED ENHANCEMENT OF USER FEE RESOURCE MANAGEMENT

FDA is committed to ensuring the sustainability of PDUFA program resources and to enhancing the operational agility of the PDUFA program. FDA will build on the financial enhancements implemented in prior authorization cycles to ensure continued optimal use of user fee resources and the alignment of staff to workload. FDA will also continue activities to promote transparency of the use of financial resources in support of the PDUFA program.

A. RESOURCE CAPACITY PLANNING

FDA will continue operating the Agency's resource capacity planning function, including modernized time reporting, to support enhanced management of PDUFA resources in PDUFA VIII and help ensure alignment of user fee resources to staff workload.

B. FINANCIAL TRANSPARENCY

1. Five-Year Financial Plan

FDA will publish a PDUFA 5-year financial plan no later than the end of the 2nd quarter of FY 2028. FDA will publish updates to the 5-year plan no later than the end of the 2nd quarter of each subsequent fiscal year. The plan and its annual updates will include the following topics:

a. **Shared Services**

i. A discussion of Agency efforts to provide Shared Services in support of the process for the review of human drug applications. Shared Services programs support Agency-wide activities (such as human resources) with costs proportionally allocated across programs, including PDUFA, based on the proportion of those costs that support the process for the review of human drug applications. This discussion will cover: the types of services that have been consolidated, the financial impact on the PDUFA program, and ongoing or planned consolidation efforts.

ii. The planned user fee obligations for FDA's Shared Services program for the five years represented by the PDUFA VIII authorization. The annual updates to this plan will provide actual amounts for the preceding fiscal year, as well as updated planned amounts for the remaining fiscal years.

iii. Discussion to address factors contributing to any variation from planned to actual amounts in excess of 10%.

b. **Index of Financial and Personnel Related Reporting**

FDA will add an appendix that will list current sources of personnel and / or financial reporting, including the financial report, performance report, and various pages on the FDA website, to explain distinctions between the personnel or other financial data provided in various reports.

2. Annual Financial Report

FDA will include the following items in the annual Financial Report submitted to Congress each year:

a. An accounting of appropriated user fee funds included in the operating reserve at the end of each fiscal year, as well as the carryover balance of user fee funds that are considered unappropriated and therefore not included in the operating reserve.

b. How any new CPA fee revenues are being allocated.

c. A discussion of the operating reserve tracking, reserving, and reporting (OR TRR), as related to section [736(g)(2)(D)] of the Food, Drug, and Cosmetic Act and FDA's objective to hire and retain staff, including:

   i. The OR TRR payroll target for the year.

   ii. A comparison of the actual payroll to the OR TRR payroll target.

   iii. A discussion of whether FDA has met the OR TRR payroll target.

   iv. If FDA has not met the OR TRR payroll target, the amounts in the operating reserve that are set aside for payroll for hiring and retaining staff.

d. In addition to the current table that provides overall PDUFA fee payroll and operating spending broken out by Center, enhanced reporting on:

   i. Personnel compensation and benefits to include payroll, awards, overtime, and benefits for personnel.

   ii. Operating expenses by major object class codes that have PDUFA fee obligations.

3. Technical Staff Meeting

FDA is committed to transparency and supporting understanding of the PDUFA program finances. FDA will commit to offering one technical staff meeting per year with regulated industry. These meetings will be expected to:

a. Occur after the publication of the fee-setting Federal Register Notice each fiscal year in the August – September timeframe, with the first meeting in 2028.

b. Include topics relevant to the fee-setting or finances of the PDUFA program.

Within 30 calendar days after the conclusion of each technical staff meeting, FDA will publish meeting minutes to its website. The meeting minutes will describe, in sufficient detail, the topics and significant points discussed in each meeting.

C. ENTERPRISE PERFORMANCE ASSESSMENT

FDA will contract with an independent third party with expertise in evaluating regulatory program operations and organizational performance to conduct a comprehensive assessment of the PDUFA program. The study will consider metrics related to the full scope of the PDUFA

program, including review, non-review, and support services for the human drug review program. The study will identify whether efficiencies have been realized and, if so, whether these efficiencies should be reflected in the PDUFA program revenue amounts.

The study will include:

a. An assessment of data and metrics available to establish a productivity baseline for all types of work. This baseline would consider staffing levels and utilization as well as the goals described in the PDUFA VIII Commitment Letter.

b. Development of a data-driven framework for assessing efficiencies of PDUFA work. The framework should evaluate both quantitative and qualitative factors.

c. Consideration of other factors of relevance related to workload, productivity, and efficiency, including but not limited to, workload, submission volume, output, timeliness, performance goals, quality, or other relevant factors.

d. An assessment of whether, considering all factors, any efficiencies achieved should be reflected in changes to the PDUFA revenue amounts.

Publication, Comment, and Decision

a. The contractor shall document its study design and methodology, findings, and recommendations in a report to be published on the FDA website.

b. By March 31, 2029, FDA will publish a report in which the contractor documents its study design and methodology, findings, and recommendations. The report will be published for public comment and on FDA's public website.

c. In the Federal Register Notice setting fees for FY 2030, FDA will publish its decision and rationale for an adjustment to be implemented, if any, including its expected schedule for fiscal years 2031 and 2032, pursuant to the adjustment described in section [736(c)(1)] of the Food, Drug, and Cosmetic Act.

    i. FDA and the regulated industry recognize that a possible outcome of this decision is no adjustment.

    ii. FDA and the regulated industry recognize that the adjustment mechanism described by section [736(c)(1)] of the Food, Drug, and Cosmetic Act is subject to renegotiation under a subsequent reauthorization of PDUFA.

III. TRANSPARENCY IN FDA HIRING AND RETENTION OF REVIEW STAFF FOR THE HUMAN DRUG REVIEW PROGRAM

The human drug review program requires that FDA maintain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of human drug applications.

During PDUFA VII, FDA experienced high attrition among technical and scientific experts involved in the review process. To deliver on PDUFA VIII commitments, FDA is committed to sharing updates on the status of restaffing the PDUFA program, including prioritizing staffing for review functions and on specific PDUFA VIII enhancements.[19]

During PDUFA VIII, FDA will share quarterly updates on PDUFA hiring via the PDUFA and BsUFA quarterly hiring webpage. FDA will also maintain the CDER and CBER net hiring webpage.

[19] To deliver on specific PDUFA VIII enhancements in Model Informed Drug Development, Rare Diseases, Facility Lifecycle Management, and Sentinel, FDA will, as part of its restaffing hiring efforts, reserve positions for certain offices in CDER (46 positions), CBER (13 positions), and OII (3 positions) during FY 2028 and will report out on the status of hiring for these enhancements in quarterly updates on FDA's webpage.

IV. INFORMATION TECHNOLOGY GOALS

A. ENHANCING TRANSPARENCY AND LEVERAGING MODERN TECHNOLOGY

FDA is committed to achieving the long-term goal of improving the exchange, review, and management of human drug and biologic applications throughout the product life cycle, and enhancing transparency, consistency, and accountability of FDA information technology (IT) and data related activities through strategic investments that support the PDUFA program.

Under PDUFA VIII, FDA will:

1. Enhance Transparency

FDA will further enhance transparency, consistency, and accountability of its data and technology modernization plans related to the regulatory submission and review process:

a. Quarterly, FDA and the regulated industry will jointly plan and conduct meetings on progress, challenges, and emerging needs for initiatives relevant to PDUFA, including continued sustainability of previous initiatives, how regulated industry input is being incorporated in these initiatives, how initiatives are enhancing the efficiency of the human drug review program (e.g., cost, speed, quality), and FDA will identify additional opportunities to collaborate with the regulated industry. Progress or activities on harmonization and convergence, where appropriate, across Center systems for streamlined compatibility, interoperability, and extensibility will also be discussed. Appropriate FDA leadership (e.g., Chief Information Officer, Chief AI Officer) will participate in at least one meeting per year. These meetings will also include discussion of the updates provided in the meeting materials, if requested by the regulated industry. The meeting materials will be shared with the regulated industry prior to each meeting. Topics of discussion are not limited to, but may include:

   i. Updates on FDA's data and technology modernization initiatives related to the regulatory submission and review process (e.g., consolidation/harmonization activities across Centers, implementation of artificial intelligence and other emerging technologies, impact of IT activities on PDUFA review commitments).

   ii. FDA efforts to ensure the usability and improvement of the ESG NextGen, including historic and current metrics on ESG NextGen performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.

   iii. Implementation of FDA's use of cloud technology to progress regulatory digital transformation (e.g., enhancements to the regulatory submission and review process to support global harmonization and collaboration efforts).

2. Feedback and Testing

With sufficient notice, FDA will provide the regulated industry with the opportunity to give feedback and/or participate in pilot testing in advance of implementing significant changes that impact the regulated industry's interaction with enterprise-wide systems.

3. Data Standards

FDA will maintain a current published FDA Data Standards Catalog and quarterly publish an updated data and technology standards action plan.

4. Promote Convergence

FDA will engage with stakeholders and international consortia (e.g., ICH, ICMRA) on technology and innovation initiatives that promote convergence in data and technology interoperability and interpretability for current and future FDA initiatives throughout the regulatory lifecycle, as well as adoption of international standards, as appropriate.

V. IMPROVING FDA PERFORMANCE MANAGEMENT

A. ASSESSMENTS WILL INCLUDE:

a. An assessment of first cycle review processes, outcomes, and FDA-sponsor communications during first cycle review, as described in section I.C.

b. An assessment of the effectiveness of two enhancements introduced in PDUFA VIII: (1) requests for written responses and face-to-face meetings, described in section I.K.2.a.ii and (2) multi-divisional meetings, described in section I.K.1.f. The assessment is described in section I.K.10.

c. An assessment of the effectiveness of the facility lifecycle program described in section I.N and the impact of the facility lifecycle program on facility-issue driven complete responses. The assessment is described in section I.N.7.

d. An enterprise performance assessment of the operations of the PDUFA program, as described in section II.C.

VI. PROGRESS REPORTING FOR PDUFA VIII AND CONTINUING PDUFA VII INITIATIVES

FDA will include in the annual PDUFA Performance Report information on the Agency's progress in meeting the specific commitments identified in this document as prescribed in statute.

FDA will include in the annual PDUFA Financial Report information identified in section II in this document and as prescribed in statute.

VII. APPENDIX: DEFINITIONS AND EXPLANATION OF TERMS

1. "Human drug applications" refers to new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act and biologics license applications submitted under section 351(a) of the Public Health Service Act, as defined in the Prescription Drug User Fee Act.[20]

2. "Human drug review program" refers to the activities to conduct "the process for the review of human drug applications," as defined in the Prescription Drug User Fee Act.[21]

3. The term "review and act on" means 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.

4. A resubmitted original application is a complete response to an action letter addressing all identified deficiencies.

5. Class 1 resubmitted applications are applications resubmitted after a complete response letter (or a not approvable or approvable letter) that include 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

    i. Other minor clarifying information (determined by the Agency as fitting the Class 1 category)

    j. Other specific items may be added and will be communicated via guidance documents to the regulated industry

[20] FD&C Act § 735(1), 21 U.S.C. § 379g(1).
[21] FD&C Act § 735(6), 21 U.S.C. § 379g(6).

6. Class 2 resubmissions are resubmissions that include any other items, including any items that would require presentation to an advisory committee.

7. The performance goals and procedures also apply to original applications and supplements for human drugs initially marketed on an over-the-counter (OTC) basis through an NDA or switched from prescription to OTC status through an NDA or supplement.

8. As used in this commitment letter, "regulatory decision making" may include, for example, FDA's process for making a regulatory decision regarding a drug or biological product throughout the product lifecycle, such as during drug development, following FDA's review of a marketing application, including review of proposed labeling for the product, or in the post-approval period (e.g., FDA's decision regarding a supplement to an approved application).