States are more likely than non-Hispanic Whites to experience heat waves, powerful hurricanes, sea level rises, and floods. It is estimated that Hispanic and Latino people are 43 percent more likely to live in an area expected to be too hot to work a full day outside due to climate change. And communities are responding. Across the United States, thousands of people have joined together to help Puerto Rico—including in Illinois—where the Puerto Rican Agenda is working to provide immediate relief to those affected by natural disasters. I support their efforts and President Biden's approval of a major disaster declaration for Puerto Rico.

Tackling environmental injustice doesn't end there. Earlier this year, activists and community leaders in southeast Chicago raised concerns with the development of a metal shredder facility. The Chicago Health Department and the Environmental Protection Agency conducted a health impact assessment, finding the metal recycling plant would have increased air pollution and negatively impacted the mental health of residents. As a result, the city blocked the development. This story is not unique to Chicago; Latino communities across the United States have mobilized to make their voices heard and protect our communities.

We also saw this tenacity during the pandemic. Millions of Hispanic and Latino people served as frontline workers—treating patients, feeding communities, and working around the clock to disinfect schools, stores, and health centers at a grave personal cost. Today, Hispanic or Latino persons are twice as likely to be hospitalized for COVID–19 and 1.8 times more likely to die from the virus, due to health disparities and continuous exposure. We must never forget the contributions they made, which have supported our Nation during one of its most difficult moments.

Countless Latino leaders have overcome systemic injustices to succeed and inspire the next generation of leaders. As we celebrate Hispanic Heritage Month, we recognize the value the Latino community brings to our country through its work and culture. Resilience and love shine through in all that the community does and will continue to make us a stronger country for years to come.

NOTICE OF A TIE VOTE UNDER S. RES. 27

Mr. PETERS. Mr. President, I ask unanimous consent to print the following letter in the RECORD.

There being no objection, the material was ordered to be printed in the RECORD, as follows:

U.S. SENATE,
COMMITTEE ON HOMELAND SECURITY AND GOVERNMENTAL AFFAIRS,
Washington, DC, September 28, 2022.

To the Secretary of the Senate:

PN 2457, the nomination of Colleen Joy Shogan, to be Archivist of the United States, vice David S. Ferriero, having been referred to the Committee on Homeland Security and Governmental Affairs, the Committee with a quorum present, has voted on the nomination as follows—

On the question of reporting the nomination favorably with the recommendation that the nomination be confirmed 7 ayes to 7 noes.

In accordance with section 3, paragraph (1)(A) of S. Res. 27 of the 117th Congress, I hereby give notice that the Committee on Homeland Security and Governmental Affairs has not reported the nomination because of a tie vote and ask that this notice be printed in the Record pursuant to the resolution.

GARY C. PETERS,
Chairman.

INFLATION REDUCTION ACT OF 2022

Ms. CORTEZ MASTO. Mr. President, I rise today to clarify a colloquy between myself and Chairman WYDEN placed in the CONGRESSIONAL RECORD on August 6, 2022. The statement in the RECORD references geothermal energy as applicable to the new ''section 48D'' of the Tax Code added by section 13702 of the Inflation Reduction Act. The statement should have referenced that section as ''section 48E.'' As explained in that colloquy, geothermal will qualify for the production and investment tax credits included in sections 13701 and 13702 of the Inflation Reduction Act.

FOOD AND DRUG ADMINISTRATION USER FEE REAUTHORIZATION

Mrs. MURRAY. Mr. President, I ask unanimous consent to have printed in the RECORD a copy of the transmittal and commitment letters from the Secretary of Health and Human Services to the chair and ranking member of the Committee on Health, Education, Labor, and Pensions of the Senate and the chair and ranking member of the Committee on Energy and Commerce of the House of Representatives regarding reauthorization of the Prescription Drug User Fee Act, Medical Device User Fee Amendments, Generic Drug User Fee Amendments, and Biosimilar User Fee Act.

There being no objection, the material was ordered to be printed in the RECORD, as follows:

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, January 12, 2022.

Hon. PATTY MURRAY,
Chair, Committee on Health, Education, Labor and Pensions, U.S. Senate, Washington, DC.

DEAR CHAIR MURRAY: The Prescription Drug User Fee Act [PDUFA] as reauthorized by the Food and Drug Administration Reauthorization Act [FDARA P.L. 115–52], expires at the end of Fiscal Year 2022. With this letter the Administration is providing our recommendations for the reauthorization of PDUFA for the Fiscal Years 2023–2027 [PDUFA VII].

Under PDUFA, the revenues generated from fees paid by the pharmaceutical industry have been used to expedite the process for the review of new prescription drugs and to support and augment regulatory science and drug development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the Food and Drug Administration [FDA] in consultation with representatives of regulated industry. FDA estimates that the fees negotiated in PDUFA VII will average approximately $1.4 billion per year. PDUFA has proven to be an extremely effective program that has transformed the U.S. drug review to be the fastest in the world, while setting the global gold standard for quality, efficacy, and safety.

Throughout this process, the FDA has solicited input and worked with various stakeholders, including representatives from consumer and patient advocates, academic research, and health provider groups, and negotiated with the pharmaceutical and biotechnology industries, to develop reauthorization recommendations for PDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site and enclosed with this letter.

Our recommendations build upon the successes of existing programs and performance goals with improvements and expansions to address areas of emerging regulatory science and drug development. For example, this includes, but is not limited to:

Investing critical resources in the Center for Biologics Evaluation and Research to support development, review, and approval of cell and gene therapy products;

Introducing new pilot programs to expedite patient access to novel uses for existing therapies, advance rare diseases development through efficacy endpoint development, and improve the quality and acceptability of real-world evidence;

Enhancing the drug safety system through optimizing the Sentinel Initiative capabilities and improving Risk Evaluation and Mitigation Strategy (REMS) assessments;

Introducing new enhancements related to product quality reviews, chemistry, manufacturing, and control approaches, and advancing the utilization of innovative manufacturing technologies;

Enhancing the use of digital health technologies to support drug development and review, along with leveraging modem technology to accelerate FDA's data and technology modernization;

Improving management of user fee resources through advancing FDA's Resource Capacity Planning function and continuing activities to enhance financial transparency.

The following five enclosures are provided for your consideration: The proposed PDUFA VII statutory language; a redline of current law; the Justifications of Proposed Statutory Changes for Reauthorization of PDUFA in Fiscal Years 2023 through 2027; the PDUFA Reauthorization Performance Goals and Procedures in Fiscal Years 2023 through 2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We would be pleased to brief your staff on the details and want to work closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accord with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH
AND HUMAN SERVICES
Washington, DC., January 12, 2022.

Hon. RICHARD BURR,
Raking Member, Committee on Health, Education, Labor and Pensions, U.S. Senate, Washington, DC.

DEAR SENATOR BURR: The Prescription Drug User Fee Act [PDUFA] as reauthorized by the Food and Drug Administration Reauthorization Act [FD ARA P. L. 115–52], expires at the end of Fiscal Year 2022. With this letter the Administration is providing our recommendations for the reauthorization of PDUFA for the Fiscal Years 2023–2027 [PDUFA VII].

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Throughout this process, the FDA has solicited input and worked with various stakeholders, including representatives from consumer and patient advocates, academic research, and health provider groups, and negotiated with the pharmaceutical and biotechnology industries, to develop reauthorization recommendations for PDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site and enclosed with this letter.

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Enhancing the drug safety system through optimizing the Sentinel Initiative capabilities and improving Risk Evaluation and Mitigation Strategy (REMS) assessments;

Introducing new enhancements related to product quality reviews, chemistry, manufacturing, and control approaches, and advancing the utilization of innovative manufacturing technologies;

Enhancing the use of digital health technologies to support drug development and review, along with leveraging modern technology to accelerate FDA's data and technology modernization;

Improving management of user fee resources through advancing FDA's Resource Capacity Planning function and continuing activities to enhance financial transparency.

The following five enclosures are provided for your consideration: The proposed PDUFA VII statutory language; a redline of current law; the Justifications of Proposed Statutory Changes for Reauthorization of PDUFA in Fiscal Years 2023 through 2027; the PDUFA Reauthorization Performance Goals and Procedures in Fiscal Years 2023 through 2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We would be pleased to brief your staff on the details and want to work closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accord with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH
AND HUMAN SERVICES,
Washington, DC, January 12, 2022.

Hon. FRANK PALLONE, JR.,
Chairman, Committee on Energy and Commerce, House of Representatives, Washington, DC.

DEAR CHAIR PALLONE: The Prescription Drug User Fee Act [PDUFA] as reauthorized by the Food and Drug Administration Reauthorization Act [FDARA P. L. 115–52], expires at the end of Fiscal Year 2022. With this letter the Administration is providing our recommendations for the reauthorization of PDUFA for the Fiscal Years 2023–2027 [PDUFA VII].

Under PDUFA, the revenues generated from fees paid by the pharmaceutical industry have been used to expedite the process for the review of new prescription drugs and to support and augment regulatory science and drug development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the Food and Drug Administration [FDA] in consultation with representatives of regulated industry. FDA estimates that the fees negotiated in PDUFA VII will average approximately $1.4 billion per year. PDUFA has proven to be an extremely effective program that has transformed the U.S. drug review to be the fastest in the world, while setting the global gold standard for quality, efficacy, and safety.

Throughout this process, the FDA has solicited input and worked with various stakeholders, including representatives from consumer and patient advocates, academic research, and health provider groups, and negotiated with the pharmaceutical and biotechnology industries, to develop reauthorization recommendations for PDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site and enclosed with this letter.

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Enhancing the use of digital health technologies to support drug development and review, along with leveraging modem technology to accelerate FDA's data and technology modernization;

Improving management of user fee resources through advancing FDA's Resource Capacity Planning function and continuing activities to enhance financial transparency.

The following five enclosures are provided for your consideration: The proposed PDUFA VII statutory language; a redline of current law; the Justifications of Proposed Statutory Changes for Reauthorization of PDUFA in Fiscal Years 2023 through 2027; the PDUFA Reauthorization Performance Goals and Procedures in Fiscal Years 2023 through 2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We would be pleased to brief your staff on the details and want to work closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accord with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH
AND HUMAN SERVICES,
Washington, DC, January 12, 2022.

Hon. CATHY MCMORRIS RODGERS,
Ranking Member, Committee on Energy and Commerce,
House of Representatives, Washington, DC.

DEAR REPRESENTATIVE MCMORRIS RODGERS: The Prescription Drug User Fee Act [PDUFA] as reauthorized by the Food and Drug Administration Reauthorization Act [FDARA P.L. 115–52], expires at the end of Fiscal Year 2022. With this letter the Administration is providing our recommendations for the reauthorization of PDUFA for the Fiscal Years 2023–2027 [PDUFA VII].

Under PDUFA, the revenues generated from fees paid by the pharmaceutical industry have been used to expedite the process for the review of new prescription drugs and to support and augment regulatory science and drug development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the Food and Drug Administration [FDA] in consultation with representatives of regulated industry. FDA estimates that the fees negotiated in PDUFA VII will average approximately $1.4 billion per year. PDUFA has proven to be an extremely effective program that has transformed the U.S. drug review to be the fastest in the world, while setting the global gold standard for quality, efficacy, and safety.

Throughout this process, the FDA has solicited input and worked with various stakeholders, including representatives from consumer and patient advocates, academic research, and health provider groups, and negotiated with the pharmaceutical and biotechnology industries, to develop reauthorization recommendations for PDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site and enclosed with this letter.

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Investing critical resources in the Center for Biologics Evaluation and Research to support development, review, and approval of cell and gene therapy products;

Introducing new pilot programs to expedite patient access to novel uses for existing therapies, advance rare diseases development through efficacy endpoint development, and improve the quality and acceptability of real-world evidence;

Enhancing the drug safety system through optimizing the Sentinel Initiative capabilities and improving Risk Evaluation and Mitigation Strategy (REMS) assessments;

Introducing new enhancements related to product quality reviews, chemistry, manufacturing, and control approaches, and advancing the utilization of innovative manufacturing technologies;

Enhancing the use of digital health technologies to support drug development and review, along with leveraging modern technology to accelerate FDA's data and technology modernization;

Improving management of user fee resources through advancing FDA's Resource Capacity Planning function and continuing activities to enhance financial transparency.

The following five enclosures are provided for your consideration: The proposed PDUFA VII statutory language; a redline of current law; the Justifications of Proposed Statutory Changes for Reauthorization of PDUFA in Fiscal Years 2023 through 2027; the PDUFA Reauthorization Performance Goals and Procedures in Fiscal Years 2023 through 2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We would be pleased to brief your staff on the details and want to work closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accord with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, May 10, 2022.

Hon. PATTY MURRAY,
Chair, Committee on Health, Education, Labor and Pensions, U.S. Senate,
Washington, DC.

DEAR CHAIR MURRAY: The Medical Device User Fee Amendments of 2017 (MDUFA IV), as reauthorized by the Food and Drug Administration Reauthorization Act (P.L. 115–52), expires at the end of Fiscal Year (FY) 2022. With this letter, the Administration is providing our recommendations for the reauthorization of MDUFA for FY 2023–2027 (MDUFA V).

Under MDUFA, the revenues generated from fees paid by the medical device industry have been used to expedite the process for the review of device applications and to support and augment regulatory science and medical device development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the U.S. Food and Drug Administration (FDA) in consultation with representatives of regulated industry.

FDA estimates that the fees negotiated in MDUFA V provide for the following five-year total revenue, prior to adjustments for inflation. They provide a minimum total revenue of approximately $1.784 billion. In addition, if specific performance goals are met in FY 2023–2025, FDA may collect up to an additional total of approximately $116 million in FY 2025–2027, for a maximum potential total of approximately $1.9 billion.

The MDUFA V package also reflects use of an additional $118 million in funding from the current MDUFA IV carryover balance to support MDUFA V activities.

Throughout this process, FDA negotiated with the regulated industry and has solicited input and worked with various stakeholders, including representatives from patient, consumer, academic research, and health provider groups, to develop reauthorization recommendations for MDUFA that would build upon and enhance the success of the program. In addition, FDA complied with the statutory requirements to solicit public comments on the draft recommendations, and the summary of public comments is posted on the agency web site.

Now pending its fourth reauthorization, MDUFA has proven to be a highly effective program for supporting the device review process. The program is designed to help ensure patient access to safe, effective, and high-quality medical devices. During the current reauthorization cycle, negotiations with industry primarily focused on: enhancements to certain performance goals; filling funding needs that had not been adequately addressed in MDUFA IV; the launch of a pilot program designed to speed patient access to certain innovative medical devices; programs to advance the development of regulatory science and to advance opportunities for patient input and collaboration in the device development process; and proposals to enhance FDA's accountability and transparency in its use of fees.

The following enclosures are provided for your consideration: the MDUFA Reauthorization Performance Goals and Procedures—Fiscal Years 2023 through 2027 (the MDUFA V Commitment Letter); a redline showing the proposed MDUFA V statutory changes compared to the current law; the Justifications of Proposed Statutory Changes for reauthorization of MDUFA in FY 2023–2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We were pleased to brief your staff on the details of the Commitment Letter and hope to continue working closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accordance with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, May 10, 2022.

Hon. RICHARD BURR,
Ranking Member, Committee on Health, Education, Labor and Pensions, U.S. Senate,
Washington, DC.

DEAR SENATOR BURR: The Medical Device User Fee Amendments of 2017 (MDUFA IV), as reauthorized by the Food and Drug Administration Reauthorization Act (P.L. 115–52), expires at the end of Fiscal Year (FY) 2022. With this letter, the Administration is providing our recommendations for the reauthorization of MDUFA for FY 2023–2027 (MDUFA V).

Under MDUFA, the revenues generated from fees paid by the medical device industry have been used to expedite the process for the review of device applications and to support and augment regulatory science and medical device development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the U.S. Food and Drug Administration (FDA) in consultation with representatives of regulated industry.

FDA estimates that the fees negotiated in MDUFA V provide for the following five-year total revenue, prior to adjustments for inflation. They provide a minimum total revenue of approximately $1.784 billion. In addition, if specific performance goals are met in FY 2023–2025, FDA may collect up to an additional total of approximately $116 million in FY 2025–2027, for a maximum potential total of approximately $1.9 billion.

The MDUFA V package also reflects use of an additional $118 million in funding from the current MDUFA IV carryover balance to support MDUFA V activities.

Throughout this process, FDA negotiated with the regulated industry and has solicited input and worked with various stakeholders, including representatives from patient, consumer, academic research, and health provider groups, to develop reauthorization recommendations for MDUFA that would build upon and enhance the success of the program. In addition, FDA complied with the statutory requirements to solicit public comments on the draft recommendations, and the summary of public comments is posted on the agency web site.

Now pending its fourth reauthorization, MDUFA has proven to be a highly effective program for supporting the device review process. The program is designed to help ensure patient access to safe, effective, and high-quality medical devices. During the current reauthorization cycle, negotiations with industry primarily focused on: enhancements to certain performance goals; filling funding needs that had not been adequately addressed in MDUFA IV; the launch of a pilot program designed to speed patient access to certain innovative medical devices; programs to advance the development of regulatory science and to advance opportunities for patient input and collaboration in the device development process; and proposals to enhance FDA's accountability and transparency in its use of fees.

The following enclosures are provided for your consideration: the MDUFA Reauthorization Performance Goals and Procedures—Fiscal Years 2023 through 2027 (the MDUFA V Commitment Letter); a redline showing the proposed MDUFA V statutory changes compared to the current law; the Justifications of Proposed Statutory Changes for reauthorization of MDUFA in FY 2023–2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We were pleased to brief your staff on the details of the Commitment Letter and hope to continue working closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accordance with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, May 10, 2022.

Hon. FRANK PALLONE, Jr.
Chairman, Committee on Energy and Commerce, House of Representatives, Washington, DC.

DEAR CHAIR PALLONE: The Medical Device User Fee Amendments of 2017 (MDUFA IV), as reauthorized by the Food and Drug Administration Reauthorization Act (P.L. 115–52), expires at the end of Fiscal Year (FY) 2022. With this letter, the Administration is providing our recommendations for the reauthorization of MDUFA for FY 2023–2027 (MDUFA V).

Under MDUFA, the revenues generated from fees paid by the medical device industry have been used to expedite the process for the review of device applications and to support and augment regulatory science and medical device development. The expenditure of these funds is in accordance with the

statute and provides resources to meet the performance goals and procedures that were developed by the U.S. Food and Drug Administration (FDA) in consultation with representatives of regulated industry.

FDA estimates that the fees negotiated in MDUFA V provide for the following five-year total revenue, prior to adjustments for inflation. They provide a minimum total revenue of approximately $1.784 billion. In addition, if specific performance goals are met in FY 2023–2025, FDA may collect up to an additional total of approximately $116 million in FY 2025–2027, for a maximum potential total of approximately $1.9 billion.

The MDUFA V package also reflects use of an additional $118 million in funding from the current MDUFA IV carryover balance to support MDUFA V activities.

Throughout this process, FDA negotiated with the regulated industry and has solicited input and worked with various stakeholders, including representatives from patient, consumer, academic research, and health provider groups, to develop reauthorization recommendations for MDUFA that would build upon and enhance the success of the program. In addition, FDA complied with the statutory requirements to solicit public comments on the draft recommendations, and the summary of public comments is posted on the agency web site.

Now pending its fourth reauthorization, MDUFA has proven to be a highly effective program for supporting the device review process. The program is designed to help ensure patient access to safe, effective, and high-quality medical devices. During the current reauthorization cycle, negotiations with industry primarily focused on: enhancements to certain performance goals; filling funding needs that had not been adequately addressed in MDUFA IV; the launch of a pilot program designed to speed patient access to certain innovative medical devices; programs to advance the development of regulatory science and to advance opportunities for patient input and collaboration in the device development process; and proposals to enhance FDA's accountability and transparency in its use of fees.

The following enclosures are provided for your consideration: the MDUFA Reauthorization Performance Goals and Procedures—Fiscal Years 2023 through 2027 (the MDUFA V Commitment Letter); a redline showing the proposed MDUFA V statutory changes compared to the current law; the Justifications of Proposed Statutory Changes for reauthorization of MDUFA in FY 2023–2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We were pleased to brief your staff on the details of the Commitment Letter and hope to continue working closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accordance with the Administration's program.

Sincerely,

XAVIER BECERRA.

Hon. CATHY MCMORRIS RODGERS,
Ranking Member, Committee on Energy and Commerce, House of Representatives, Washington, DC.

DEAR REPRESENTATIVE MCMORRIS RODGERS: The Medical Device User Fee Amendments of 2017 (MDUFA IV), as reauthorized by the Food and Drug Administration Reauthorization Act (P.L. 115–52), expires at the end of Fiscal Year (FY) 2022. With this letter, the Administration is providing our recommendations for the reauthorization of MDUFA for FY 2023–2027 (MDUFA V).

Under MDUFA, the revenues generated from fees paid by the medical device industry have been used to expedite the process for the review of device applications and to support and augment regulatory science and medical device development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the U.S. Food and Drug Administration (FDA) in consultation with representatives of regulated industry.

FDA estimates that the fees negotiated in MDUFA V provide for the following five-year total revenue, prior to adjustments for inflation. They provide a minimum total revenue of approximately $1.784 billion. In addition, if specific performance goals are met in FY 2023–2025, FDA may collect up to an additional total of approximately $116 million in FY 2025–2027, for a maximum potential total of approximately $1.9 billion.

The MDUFA V package also reflects use of an additional $118 million in funding from the current MDUFA IV carryover balance to support MDUFA V activities.

Throughout this process, FDA negotiated with the regulated industry and has solicited input and worked with various stakeholders, including representatives from patient, consumer, academic research, and health provider groups, to develop reauthorization recommendations for MDUFA that would build upon and enhance the success of the program. In addition, FDA complied with the statutory requirements to solicit public comments on the draft recommendations, and the summary of public comments is posted on the agency web site.

Now pending its fourth reauthorization, MDUFA has proven to be a highly effective program for supporting the device review process. The program is designed to help ensure patient access to safe, effective, and high-quality medical devices. During the current reauthorization cycle, negotiations with industry primarily focused on: enhancements to certain performance goals; filling funding needs that had not been adequately addressed in MDUFA IV; the launch of a pilot program designed to speed patient access to certain innovative medical devices; programs to advance the development of regulatory science and to advance opportunities for patient input and collaboration in the device development process; and proposals to enhance FDA's accountability and transparency in its use of fees.

The following enclosures are provided for your consideration: the MDUFA Reauthorization Performance Goals and Procedures—Fiscal Years 2023 through 2027 (the MDUFA V Commitment Letter); a redline showing the proposed MDUFA V statutory changes compared to the current law; the Justifications of Proposed Statutory Changes for reauthorization of MDUFA in FY 2023–2027; and the summary of public comments.

Thank you for the opportunity to present our recommendations to reauthorize this vital program. We were pleased to brief your staff on the details of the Commitment Letter and hope to continue working closely with Congress to reauthorize the program in a timely manner. The Office of Management and Budget has advised that the bill and the enclosed performance goals are in accordance with the Administration's program.

Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, January 12, 2022.

Hon. PATTY MURRAY,
Chair, Committee on Health, Education, Labor and Pensions,
U.S. Senate, Washington, DC.

DEAR CHAIR MURRAY: The Generic Drug User Fee Amendments of 2017 [GDUFA II], as reauthorized by the Food and Drug Administration Reauthorization Act [FDARA P. L. 115–52], expires at the end of Fiscal Year 2022. With this letter, the Administration is providing our recommendations for the reauthorization of GDUFA for the Fiscal Years 2023–2027 [GDUFA III].

Under GDUFA, the revenues generated from fees paid by the generic pharmaceutical industry have been used to expedite the process for the review of generic drugs and to support and augment regulatory science and generic drug development. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the Food and Drug Administration [FDA] in consultation with representatives of regulated industry. FDA estimates that the fees negotiated in GDUFA III will be over $600 million per year, adjusted annually for inflation.

Throughout this process, FDA has solicited input and worked with various stakeholders, including representatives from consumer, patient, academic research, and health provider groups, and negotiated with the regulated industry, to develop reauthorization recommendations for GDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site.

Our recommendations build upon the successes of existing programs and performance goals with enhancements to advance approvals in fewer review cycles, proposals to enhance regulatory science and expedite complex generic drug development, and financial proposals to support the generic drug program as it evolves. For example, minimizing the issuance of complete response letters through the use of ''imminent actions'' to approve an application within 60 days after the goal date will reduce the number of review cycles. The pre-ANDA program, which was initiated as part of GDUFA II, has several enhancements, including new goal dates for Product-Specific Guidances [PSGs] that expedite complex generic drug development. The proposals also include improvements for FDA to enhance the operational agility of the GDUFA program through maturation of the Resource Capacity Planning (RCP) capability and the proposed implementation of a Capacity Planning Adjustment (CPA) in fee-setting to generally allow for up to a three percent increase in inflation-adjusted target revenue for the upcoming fiscal year if sustained increases in the workload are predicted, using a methodology developed and evaluated during GDUFA II.

The following five enclosures are provided for your consideration: the proposed GDUFA III statutory language; a redline of these changes compared to the current law; the Justifications of Proposed Statutory Changes for reauthorization of GDUFA in Fiscal Years 2023 through 2027; the GDUFA Reauthorization Performance Goals and Procedures—Fiscal Years 2023 through 2027 [the GDUFA III Commitment Letter]; and the summary of public comments.

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Sincerely,

XAVIER BECERRA.

THE SECRETARY OF HEALTH AND HUMAN SERVICES,
Washington, DC, January 12, 2022.

Hon. RICHARD BURR,
Ranking Member, Committee on Health, Education, Labor and Pensions,
U.S. Senate, Washington, DC.

DEAR SENATOR BURR: The Generic Drug User Fee Amendments of 2017 [GDUFA II], as reauthorized by the Food and Drug Administration Reauthorization Act [FDARA P.L. 115–52], expires at the end of Fiscal Year 2022. With this letter, the Administration is providing our recommendations for the reauthorization of GDUFA for the Fiscal Years 2023–2027 [GDUFA III].

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Throughout this process, FDA has solicited input and worked with various stakeholders, including representatives from consumer, patient, academic research, and health provider groups, and negotiated with the regulated industry, to develop reauthorization recommendations for GDUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site.

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Hon. PATTY MURRAY,
Chair, Committee on Health, Education, Labor and Pensions,
U.S. Senate, Washington, DC.

DEAR CHAIR MURRAY: The Biosimilar User Fee Act [BsUFA] as reauthorized by the FDA Reauthorization Act of 2017 [Pub. L. 115–52], expires at the end of Fiscal Year 2022. With this letter the Administration is providing our recommendations for the reauthorization of BsUFA for the Fiscal Years 2023–2027 [BsUFA III].

Under BsUFA, the revenues generated from fees paid by the pharmaceutical industry have been used to support the process for the review of biosimilar biological products. The expenditure of these funds is in accordance with the statute and provides resources to meet the performance goals and procedures that were developed by the Food and Drug Administration [FDA] in consultation with representatives of regulated industry. FDA estimates that the fees negotiated in BsUFA III will average approximately $51 million per year.

As part this process, the FDA has negotiated with the pharmaceutical and biotechnology industries to develop reauthorization recommendations for BsUFA that would build upon and enhance the success of the program. In addition, we have complied with the statutory requirements to solicit public comments on our recommendations, and the summary of public comments is posted on the agency web site and enclosed with this letter.

Our recommendations build upon the successes of the BsUFA program by refining elements of the existing program and including new enhancements where appropriate. For example, these recommendations include, but are not limited to:

Introducing new supplement categories, review timelines, and performance goals to expedite the review of certain supplements, including safety labeling updates

Advancing the development of safe and effective interchangeable biosimilar biological products through foundational guidance development, stakeholder engagement, and other activities

Piloting a regulatory science program focused on enhancing regulatory decisionmaking and facilitating science-based recommendations in areas foundational to biosimilar and interchangeable biological product development

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PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027

PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027

This document contains the performance goals and procedures for the Prescription Drug User Fee Act (PDUFA) reauthorization for fiscal years (FYs) 2023–2027, known as PDUFA VII. 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 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 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 VII. 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).

I. ENSURING THE EFFECTIVENESS OF THE HUMAN DRUG REVIEW PROGRAM

A. REVIEW PERFORMANCE GOALS

1. NDA/BLA Submissions and Resubmissions

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.

c. Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt.

d. Review and act on 90 percent of priority non-NME original NDA submissions within 6 months of receipt.

e. Review and act on 90 percent of Class 1 resubmitted original applications within 2 months of receipt.

f. Review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

2. Original Efficacy Supplements

a. Review and act on 90 percent of standard efficacy supplements within 10 months of receipt.

b. Review and act on 90 percent of priority efficacy supplements within 6 months of receipt.

3. Resubmitted Efficacy Supplements

a. Review and act on 90 percent of Class 1 resubmitted efficacy supplements within 2 months of receipt.

b. Review and act on 90 percent of Class 2 resubmitted efficacy supplements within 6 months of receipt.

4. Original Manufacturing Supplements

a. Review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

b. Review and act on 90 percent of all other manufacturing supplements within 6 months of receipt.

5. 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.

6. These review goals are summarized in the following tables:

TABLE 1

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	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 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

	Prior Approval	All Other
Manufacturing Supplements	90% in 4 months of the receipt date	90% in 6 months of the receipt date

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, 2022, through September 30, 2027. 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 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.e and I.A.1.f 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. 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.E).

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:

1. risk management,

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

3. 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) 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:

1. 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.

2. 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.

3. 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.

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

FDA will establish the following pre-approval process enhancements and guidelines in PDUFA VII:

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 phased in, starting in FY 2023 as follows:

a. In FY 2023, communicate anticipated PMRs to the applicant no later than 8 weeks prior to the PDUFA action goal date for 60% of standard NME NDAs and original BLAs.

b. In FY 2024, communicate anticipated PMRs to the applicant no later than 8 weeks prior to the PDUFA action goal date for 70% of standard NME NDAs and original BLAs.

c. In FY 2025, 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.

d. In FY 2026, 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.

e. In FY 2027, 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 phased in, starting in FY 2023 as follows:

a. In FY 2023, communicate anticipated PMRs to the applicant no later than 6 weeks prior to the PDUFA action goal date for 60% of priority NME NDAs and original BLAs.

b. In FY 2024, communicate anticipated PMRs to the applicant no later than 6 weeks prior to the PDUFA action goal date for 70% of priority NME NDAs and original BLAs.

c. In FY 2025, 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.

d. In FY 2026, 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.

e. In FY 2027, 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.

In addition, FDA will enhance clarity and transparency for the NME Review Program by updating all relevant Manuals of Policies and Procedures (MAPPs), Standard Operating Procedures and Policies (SOPPs), and guidances regarding the pre-approval processes for establishing PMRs beginning FY 2023 and finalizing by the end of FY 2027. The Agency will also conduct training for all relevant review and program support staff on updated processes related to postmarketing studies beginning FY 2023, including:

a. Preliminary communication with applicants at mid-cycle for PMRs, PMCs, and REMS.

b. Processes and procedures for ARIA sufficiency determination.

2. Post-approval review of existing PMRs: In addition to mechanisms currently 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 establish an additional process for reviewing 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 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 will be incorporated into all relevant MAPPs, SOPPs, and guidances beginning FY 2023 and finalizing by the end of FY 2027 and will not be PDUFA-tracked metrics or subject to performance goals.

D. Split Real Time Application Review (STAR) Pilot Program

FDA will establish a STAR pilot program, which has the goal of shortening the time from the date of complete submission to the action date, in order to allow earlier patient access to therapies that address an unmet medical need. The STAR pilot program will apply to efficacy supplements across all therapeutic areas and review disciplines that meet specific criteria. Accepted STAR applications will be submitted in a ''split'' fashion, specifically in two parts (with the components submitted approximately 2 months apart).

1. Scope: The STAR program will seek to expedite patient access to novel uses for existing therapies by supporting initiation of review earlier than would otherwise occur and therefore allowing earlier approval for qualified efficacy supplements. This program will apply across all therapeutic areas and review disciplines for applications that meet specific criteria. An application will be considered eligible for STAR if each of the following criteria are met:

a. Clinical evidence from adequate and well-controlled investigation(s) indicates that the drug may demonstrate substantial improvement on a clinically relevant endpoint(s) over available therapies.

i. Breakthrough Therapy Designation (BTD) or Regenerative Medicine Advanced Therapy Designation (RMAT) is not required, but above criteria must be met.

b. The application is for a drug intended to treat a serious condition with an unmet medical need.

c. No aspect of the submission is likely to require a longer review time (e.g., requirement for new REMS, etc.).

d. There is no chemistry, manufacturing, or control information that would require a foreign manufacturing site inspection (i.e., domestic site inspections may be allowed if it does not affect the expedited timeframe).

2. Process and Timeline: The following steps summarize the process for applying to and participating in the STAR program:

a. An applicant who believes an efficacy supplement qualifies for review under the STAR program will request an informal pre-submission teleconference with FDA and provide FDA with topline trial results and proposed labeling.

i. Alternatively, the preliminary discussion may take place as part of a pre-sNDA/sBLA meeting.

b. If FDA agrees that the pre-submission request meets the STAR program eligibility criteria, the application will be accepted into the STAR program, and the applicant will agree to provide the complete application in two parts (these two parts are described in the Split Submission Components section below or as agreed to with the Review Division).

c. FDA will initiate review of the data upon receipt of the Part 1 submission.

d. The PDUFA timeline will begin upon receipt of the Part 2 submission (which completes the application). FDA intends to follow the expedited review timelines (as described in Section I.E below). These timelines target taking an action at least 1 month earlier than the applicable PDUFA goal date.

e. The filing meeting will be scheduled within 30 days of FDA's receipt of the Part 2 submission. During the filing meeting, FDA will determine an action date at least 1 month in advance of the priority 6-month PDUFA goal date.

i. FDA will notify the applicant of the intended action date in the filing letter. The PDUFA goal date will remain unchanged.

3. Split Submission Components: Applications reviewed under the STAR program will comprise two separate submissions.

a. The Part 1 submission initiates FDA's review and will contain:

i. All components of the NDA/BLA efficacy supplement (e.g., complete datasets, proposed labeling, clinical protocols and amendments, topline efficacy and safety results), except for final clinical study reports for the adequate and well-controlled investigation(s) supporting the proposed claim and the eCTD module 2 clinical summaries, and

ii. A document providing topline results for each of the adequate and well-controlled investigations will also be provided in the Part 1 submission.

Any modifications to submission content are at the discretion of the OND/CDER clinical division or CBER review office and must be agreed to in advance.

b. The Part 2 submission initiates the PDUFA timeline and will contain:

i. The clinical study reports for the adequate and well-controlled investigation(s) (e.g., Phase 3 studies) intended to support the proposed indication, and

ii. The eCTD module 2 clinical summaries not included in the Part 1 submission.

Part 1 will be submitted approximately 2 months, and not longer than 3 months, in advance of Part 2. If the Part 1 submission is incomplete (i.e., it does not include every component described in Section D.3.a. above, except for easily correctable minor deficiencies of components not essential to initiating review, as determined by the OND/CDER division or CBER review office), the review will not be initiated until the application is complete and the application will no longer be considered within the STAR program.

4. Transparency: The Agency will develop a public-facing webpage outlining detailed criteria for potential acceptance and participation in the STAR program by October 1, 2022. FDA will conduct an interim assessment that includes internal activities related to STAR by the end of FY 2025. FDA will also conduct a public workshop by the end of Q2 in FY 2026 to discuss the potential value and feasibility of expanding the pilot program to select NME NDAs and BLAs and solicit feedback on experiences with the pilot program

from industry stakeholders. Outputs from the assessment and workshop will be published in a publicly available report summarizing both overall metrics for the pilot program and external stakeholder feedback, including the percentage of applications accepted into the program based on the number of requests and the percentage of applications that had an action date at least 1 month in advance of the priority 6–month PDUFA goal date. FDA will also commit to training review staff on STAR processes and providing a publicly available report summarizing training activities conducted.

5. Implementation: The STAR program will be available to applicants beginning in FY 2023. Expediting reviews will be fully implemented by FY 2024 to allow time for FDA to hire necessary staff to support the expedited timeline.

E. Expedited Reviews

The term ''expedited review'' in this letter refers to FDA's review of either 1) 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, or 2) an efficacy supplement in the STAR pilot program, 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 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. In 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. In 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. In 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. In 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. N.B. 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. N.B. 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. Meeting Management Goals

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.

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.

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.

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

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:

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);

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

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.

1. 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 cuttingedge 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.

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

i. 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).

ii. 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:

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

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

3) 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;

4) 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;

5) 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

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

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.

TABLE 3

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 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, 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. When it is determined 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. If the sponsor believes a face-to-face Pre-IND meeting is valuable and warranted, then the sponsor may provide a rationale in a follow-up correspondence explaining why a face-to-face meeting is valuable and warranted, and FDA will convert where possible WRO to a face-to-face meeting for requests that includes novel approaches to clinical development and/or where precedents are not well established.

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

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:

i. Type A, B, B(EOP) and C 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.

ii. Type D meeting: performance goals for FDA will be phased in, starting in FY 2023 as follows:

1) By FY 2023, hold 50% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.

2) By FY 2024, hold 60% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.

3) By FY 2025, hold 70% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.

4) By FY 2026, hold 80% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.

5) By FY 2027, hold 90% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.

INTERACT meeting: performance goals for FDA will be phased in, starting in FY 2023 as follows:

1) By FY 2023, hold 50% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

2) By FY 2024, hold 60% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

3) By FY 2025, hold 70% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

4) By FY 2026, hold 80% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

5) By FY 2027, hold 90% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

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

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	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), D, INTERACT, or C 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. 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, 2023, FDA will issue a revised draft of the existing draft guidance on ''Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products'' with information pertaining to INTERACT, Type D meetings, and the follow-up opportunity described below. 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 will develop criteria and parameters for permissible requests, and 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.

c. Training: FDA will conduct external training to ensure the best practices outlined in the draft guidances are communicated to Industry.

K. Enhancing Regulatory Science and Expediting Drug Development

To ensure that new and innovative products are developed and available to patients in a timely manner, FDA will continue to advance the use of biomarkers and pharmacogenomics, enhancing communications between FDA and sponsors during drug development, and advancing the development of drugs for rare diseases. The extension and continuation of this work will encompass further evaluation and enhancement of FDA-sponsor communications, ensuring the sustained success of the breakthrough therapy program, continuing early consultations between FDA and sponsors on the use of new surrogate endpoints as the primary basis for product approval, advancing rare disease drug development, advancing the development of combination products, and exploring the use of real world evidence for use in regulatory decision-making.

1. Promoting Innovation Through Enhanced Communication Between FDA and Sponsors During Drug Development

FDA's philosophy is that timely interactive communication with sponsors during drug development is a core Agency activity to help achieve the Agency's mission 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. Accordingly, FDA will maintain dedicated drug development communication and training staffs in CDER and CBER, focused on enhancing communication between FDA and sponsors during drug development.

One function of the staff is to serve as a liaison that will facilitate general and, in some cases, specific interactions between sponsors and each Center. The liaison will serve as a point of contact for sponsors who have general questions about drug development or who need clarification on which review division to contact with their questions. The liaison will also serve as a secondary point of contact in each Center for sponsors who are encountering challenges in communication with the review team for their IND (e.g., in instances when they have not received a response from the review team to a simple or clarifying question or referral to the formal meeting process within 30 days of the sponsor's initial request). In such cases, the liaison will work with the review team and the sponsor to facilitate resolution of the issue.

The second function of the staff is to provide ongoing training to the review organizations on best practices in communication with sponsors. The content of training includes, but is not limited to, FDA's philosophy regarding timely interactive communication with sponsors during drug development as a core Agency activity, best practices for addressing sponsor requests for advice and timely communication of responses through appropriate mechanisms (e.g., teleconferences, secure email, or when questions are best addressed through the formal meetings process), and the role of the liaison staff in each Center in facilitating communication between the review staff and sponsor community, including the staff's role in facilitating resolution of individual communication requests. The staff will also collaborate with sponsor stakeholders (e.g., through participation in workshops, webinars, and other meetings) to communicate FDA's philosophy and best practices regarding communication with sponsors during drug development.

Best Practices for meetings are the responsibility of both Industry and FDA. Efforts from both Industry and FDA are needed in order to continue advancement, improvement, and updating of best practices. To continue to enhance timely interactive communication with sponsors during drug development in PDUFA VII, FDA will do the following:

a. Public Workshop. FDA will hold a public meeting to discuss best practices for meeting management by July 30, 2024, including issues related to submission of meeting requests, efficient time management, coordinating meeting agenda, development and submission of meeting background packages and lessons learned from the Coronavirus Disease 2019 (''COVID–19'') pandemic including virtual meeting platforms. Learnings from the public meeting could inform FDA's internal process improvement efforts and, as appropriate, be reflected in updating guidances, as noted below. This public workshop will also discuss and share experience and metrics related to all PDUFA meeting activities, including Type D and INTERACT meetings. FDA will discuss the number of meeting requests granted and denied for INTERACT meetings, including a summary of rationales for denied meeting requests. Reported metrics will include the number of requests granted and denied for in-person pre-IND, Type C, Type D, and INTERACT meetings. FDA and Industry will agree on the information that FDA may share publicly in this meeting.

b. Guidance. Based on the discussion at the public meeting mentioned above in paragraph (a), and FDA's experience with conducting meetings effectively, FDA will update public documents, as appropriate, including publishing revised draft or final version of the Best Practices for Communication Between IND Sponsors and FDA During Drug Development guidance mentioned below, 18 months after the public meeting is held.

c. Training. FDA will conduct external training to ensure the best practices outlined in the guidances are communicated to Industry.

2. 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. 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. 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.

3. Early Consultation on the Use of New Surrogate Endpoints

FDA and 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 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.J of this document will apply.

4. 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 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 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) Pilot 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.

Current mechanisms for sponsors of rare disease drug development programs to collaborate with FDA are not structured to provide repeated, intensive interactions with the Agency. To support the advancement of rare disease treatments, FDA will establish a pilot program 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. In addition, FDA will 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.

Scope. The RDEA pilot 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 proposal submission to 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.

(3) FDA will select a limited number of qualified proposals for admission into RDEA that increases after the first year of PDUFA VII:

(a) FY 2023: Sponsors may submit proposals beginning in Q4, and FDA will accept a maximum of 1 proposal.

(b) FY 2024–FY 2027: FDA will accept up to 1 proposal per quarter with a maximum of 3 proposals per year.

(c) Expansion of the program may be dependent on FDA staffing.

Process and Timeline. 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, relevant summaries of pertinent information related to the endpoint from prior studies, as well as a statement indicating if the company is willing to allow disclosure of information for broader development and educational purposes.

(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) Before FDA grants the initial meeting, FDA and the sponsor will agree on the information that FDA may share publicly. When feasible, FDA will notify a sponsor in advance when the sponsor's program is the planned focus of a public discussion. Participation in the pilot program, including such agreement on information disclosure, will be voluntary and at the discretion of the sponsor. If FDA and the sponsor of an accepted proposal are unable to reach agreement on elements for public disclosure, however, that proposal will no longer be part of the RDEA pilot program and the Agency will proceed with an alternate submission.

(5) Sponsors admitted to the RDEA pilot may participate in up to 4 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 45 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.

(6) Sponsors who have completed the maximum of 4 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 nonbinding. Completing the 4 RDEA meetings does not guarantee approval for a regulatory submission that includes efficacy endpoints discussed during RDEA meetings.

(b) After completion of 4 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.

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

iii. Transparency and Endpoint Advancement. As part of RDEA, FDA will conduct up to 3 public workshops by the end of FY 2027 to discuss various topics relevant to endpoint development for rare diseases, such as the use of multidomain analysis methods. 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, including prior to FDA's approval for the drug studied in the trial. However, as noted above, before FDA grants the initial RDEA meeting the Agency and the sponsor will agree on the information that FDA may share publicly in these case studies. When feasible, FDA will notify a sponsor in advance when the sponsor's program is the planned focus of a public discussion.

5. 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 goals for FDA will be phased in, starting FY 2024 as follows:

1) By FY 2024, review and notify sponsor of agreement or non-agreement with comments for 50% of filed submissions, within 60 days of receipt of submission.

2) By FY 2025, review and notify sponsor of agreement or non-agreement with comments for 70% of filed submissions, within 60 days of receipt of submission.

3) By FY 2026, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.

4) By FY 2027, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.

iv. By the end of FY 2024, FDA will publish new draft or revised guidance for review staff and industry describing considerations related to drug-device and biologic-device combination products on the topics noted below.

Guidance that will convey FDA's current thinking regarding how a URRA along with other information can be used to inform when the results from an HF validation study may need to be submitted to a marketing application. The guidance will provide a comprehensive, systematic and stepwise approach with examples, when applicable, to illustrate how to make this determination.

v. Sponsors may still elect to submit a URRA with a HF validation protocol and will only be subject to timelines in Section I.K.5.b, For Human Factor Validation Study Protocols.

b. For Human Factor 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:

i. Beginning in FY 2023, review and provide sponsor with written comments for 90% of human factors validation protocol submissions within 60 days of receipt of protocol submission.

6. Advancing Real-World Evidence for Use in Regulatory Decision-Making

In accordance with Section 3022 of the 21st Century Cures Act, and by providing earlier and increased Agency advice, the Advancing RWE Program seeks to improve the quality and acceptability of RWE-based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements. Specifically, FDA will do the following:

a. By no later than December 31, 2022, FDA will establish and communicate publicly a pilot Advancing RWE Program intended to:

i. Identify approaches for generating RWE that meet regulatory requirements in support of labeling for effectiveness (e.g., new indications, populations, dosing information) or for meeting post-approval study requirements;

ii. Develop agency processes that promote consistent decision-making and shared learning regarding RWE;

iii. Promote awareness of characteristics of RWE that can support regulatory decisions by allowing FDA to discuss study designs considered in the Advancing RWE Program in a public forum.

b. The Advancing RWE Program will include but not be limited to the following activities and components:

i. FDA will solicit applications for the Advancing RWE Program twice (i.e., two cycles) each year, asking sponsors to describe—before protocol development or study initiation—the regulatory question(s) they seek to address with RWE, the proposed RWE study design, and the potential real-world data (RWD) source(s) to support that design;

ii. FDA will use a structured review process to evaluate and rank applications, based on the information they present that the data may be fit-for-use, the study design will be adequate, and the proposed study conduct can be anticipated to meet regulatory requirements. Consideration will be given to promoting diversity of data sources, study designs, analytical methodologies and regulatory indications, as well as to diversity of diseases under study and FDA Centers and Offices involved;

iii. FDA will accept one to two eligible and appropriate proposals each cycle in the first and second year (FY 2023–2024) of the Advancing RWE Program and one to four eligible and appropriate proposals each cycle thereafter (FY 2025–2027);

iv. FDA will notify sponsors regarding acceptance or non-acceptance of their submission within 45 days of the application deadline;

v. FDA will convene the first of up to four dedicated Advancing RWE Program meetings within 75 days of the application deadline, with subsequent meetings to be scheduled within 45 days after receiving a request for such meetings from the sponsor;

vi. The Advancing RWE Program represents an optional pathway for sponsors

submitting RWE proposals to an IND with CDER or CBER. Regardless of whether an Advancing RWE application is accepted, not accepted, or was never submitted to the Advancing RWE Program, established procedures (e.g., formal PDUFA meetings with the review division) will continue to be available;

vii. Before FDA grants the initial meeting, FDA and the sponsor will agree on the information that FDA may share publicly. When feasible, FDA will notify a sponsor in advance when the sponsor's program is the planned focus of a public discussion. Participation in the pilot program, including such agreement on information disclosure, will be voluntary and at the discretion of the sponsor;

viii. If FDA and the sponsor of an accepted proposal are unable to reach agreement on elements for public disclosure, however, that proposal will no longer be part of the Advancing RWE Program and the Agency will proceed with an alternate submission (The timelines for meetings described above would shift based on the dates of accepting alternate submissions, if applicable.);

ix. Discussions at Advancing RWE program-related meetings will focus on data, design, and regulatory issues that have the potential to generate RWE in support of a proposed regulatory decision;

x. FDA participation in the Advancing RWE Program, including the selection process and program-related meetings, will include representatives from relevant review divisions, other offices with RWE expertise, and senior leadership with expertise in RWE;

xi. Sponsors and FDA can decide that four meetings may not be necessary if an agreed-upon protocol is identified. Conversely, if FDA determines that key data- or design-related problems make the protocol unlikely to support the intended regulatory decision, then subsequent meetings within the Advancing RWE Program may not be conducted;

xii. FDA and sponsors agree that the goal of the Advancing RWE Program is general agreement on key design elements. The acceptability of evidence generated from any completed study is a subsequent review issue;

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

c. By no later than June 30, 2024, FDA will 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). This reporting will include but not be limited to protocols emerging from the Advancing RWE Program.

d. By no later than December 31, 2025, FDA will convene a public workshop or meeting to discuss RWE case studies with a particular focus on approaches for generating RWE that can potentially meet regulatory requirements in support of labeling for effectiveness (e.g., new indications, populations, dosing information) or for meeting post-approval study requirements.

e. By no later than December 31, 2026, experience gained with the Advancing RWE Program, as well as CDER's and CBER's RWE program in general, will be used to update existing RWE-related guidance documents or generate new draft guidance, as appropriate.

L. Enhancing Regulatory Decision Tools to Support Drug Development and Review

Delivering new medicines to patients through biomedical innovation requires advances in regulatory decision tools to support drug development and review. FDA will build on the successes of its efforts on Patient Focused Drug Development (PFDD), benefit-risk assessment in regulatory decision-making, and the drug development tools qualification pathway for biomarkers. FDA will also continue to advance modern approaches to enhance the efficiency of the drug development and review processes, such as complex adaptive, Bayesian, and other novel clinical trial designs and model-informed drug development (MIDD).

1. Enhancing the Incorporation of the Patient's Voice in Drug Development and Decision-Making

To facilitate the advancement and use of systematic approaches to collect and utilize robust and meaningful patient and caregiver input that can more consistently inform drug development and, as appropriate, regulatory decision making, FDA will conduct the following activities during PDUFA VII:

a. FDA will continue to strengthen capacity to facilitate development and use of Patient-Focused methods to inform drug development and regulatory decisions. This includes expanded internal staff training and external outreach to industry sponsors and other involved stakeholders with emphasis on patient-focused drug development (PFDD) methods and tools-related guidance and practice to achieve broad acceptance and integration into regulatory decision making across review divisions and industry development programs. FDA will also engage external experts, through a mechanism called the Intergovernmental Personnel Act, to support the review of patient experience data. These external methodological experts will possess extensive knowledge in methods and approaches related to patient experience data and will augment existing internal expertise.

i. FDA will undertake a broad-based effort to conduct outreach and training across review divisions, with follow-up consultation as these methods gain broad acceptance and integration, including development of methodology training courses for review staff that will be conducted at least two times per year.

ii. FDA will conduct targeted outreach to industry and methodological consulting organizations to provide presentations, sessions, and resources to increase understanding, acceptance, and integration into development programs.

b. FDA will issue a Request for Information (RFI) to elicit public input on methodological issues, including the submission and evaluation of patient experience data in the context of the benefit-risk assessment and product labeling, and other areas of greatest interest or concern to public stakeholders. This RFI will be issued by no later than the end of June 2023.

i. FDA will issue a Federal Register Notice summarizing the input to the RFI by no later than the end of December 2023 and, based on the input received in response to the RFI, FDA will plan to conduct at least 2 public workshops focused on methodological issues.

ii. The first workshop will be held no later than the end of FY 2024.

iii. The second workshop will be held no later than the end of FY 2025.

iv. Based on the RFI and the learnings from the workshops, FDA will produce a written summary with identified priorities for future work no later than the end of FY 2026.

c. FDA will continue to work to develop a virtual catalog of standard core sets of Clinical Outcome Assessments (COAs) and Related Endpoints, pursuing non-user fee funding for the work to develop standard core sets, which will be available for public use. FDA will also work to enhance understanding of how patient preference informs meaningful benefit or benefit-risk tradeoffs in therapeutic areas.

d. A public input process through either the Federal Register or Public Meetings will allow FDA to understand stakeholder's perspectives on diseases and domains of greatest need or highest priority for development of Standard Core COAs and Endpoints as well as priority areas where decisions are preference-sensitive and patient preference information (PPI) data can inform regulatory decision-making.

e. By September 30, 2026, FDA will publish draft guidance on use and submission of patient preference information to support regulatory decision making. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

2. 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. 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. CBER incorporates benefit-risk assessment through interdisciplinary review and has integrated the Benefit-Risk Framework into its clinical review template for its new BLA and supplement assessments. CDER has similarly integrated the Benefit-Risk Framework into its clinical review and decisional memo templates.

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.

3. Advancing Model-Informed Drug Development

FDA will build on the success of the ''model-informed drug development'' (MIDD) approaches by continuing to advance and integrate the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources in drug development and regulatory review. FDA will conduct the following activities during PDUFA VII:

a. By no later than the end of 1st Quarter of FY 2023, FDA will publish a Federal Register Notice announcing the continuation of the MIDD paired meeting program, outlining program eligibility, and describing the proposal submission and selection process.

b. For sponsors participating in the MIDD paired meeting program, FDA will grant a pair of meetings specifically designed for this program, consisting of an initial and a follow-up meeting on the same drug development issues. The second meeting will occur within approximately 60 days of receiving the briefing materials. These meetings will be led by the clinical pharmacology or biostatistical review components within CDER

or CBER in partnership with clinical staff at the relevant center to ensure alignment with decision makers.

c. Starting in FY 2023, FDA will select 1–2 eligible and appropriate proposals per quarter each year (i.e. up to 8 per year). Additional proposals that meet the eligibility criteria may be selected depending upon the availability of resources. The internal review group instituted by FDA will continue to review proposals on a quarterly basis and provide recommendations on prioritization and selection of proposals and share knowledge and experience.

d. Sponsors who do not participate in the MIDD paired meeting program will have an opportunity to interact with the Agency through traditional channels.

e. FDA will issue a Request for Information (RFI) to elicit public input for identifying priority focus areas for future policy or guidance development and stakeholder engagement. This RFI will be issued by no later than the end of FY 2024.

4. Enhancing Capacity to Review Complex Innovative Designs

To facilitate the advancement and use of complex adaptive, Bayesian, and other novel clinical trial designs, FDA will conduct the following activities during PDUFA VII:

a. FDA will continue to develop CDER and CBER staff capacity to enable processes to facilitate appropriate use of these types of methods. This staff will support the computationally intensive review work necessary to evaluate complex adaptive, Bayesian, and other novel clinical trial designs, with a particular focus on clinical trial designs for which simulations are necessary to evaluate the operating characteristics. FDA will also engage external experts through existing FDA mechanisms (e.g., Intergovernmental Personnel Act assignment) to support the review of complex innovative designs. These methodological experts will possess extensive knowledge in the aforementioned topics and will augment existing internal expertise.

b. FDA will maintain the paired meeting program, selecting 1–2 eligible and appropriate proposals per quarter each year (i.e. up to 8 per year) for highly innovative trial designs for which analytically derived properties (e.g., Type I error) may not be feasible, and simulations are necessary to determine trial operating characteristics. Additional proposals that meet the eligibility criteria may be selected depending upon the availability of resources. For INDs in the program, FDA will grant a pair of meetings, consisting of an initial and follow-up meeting on the same design. The second meeting will occur within approximately 90 days of receiving the briefing materials. Management of the overall program as well as specific meetings to discuss innovative designs will be led by the biostatistical review components within CDER or CBER in partnership with clinical staff at each center. The opportunity for increased interaction with the agency will provide better understanding of the agency's requirements for trial simulations involved in the use of the pilot study design and allow for iteration of design modifications, if needed. In return, FDA's ability to publicly discuss example designs as agreed upon with participating sponsors will provide better clarity on the acceptance of different types of trial designs that should facilitate their use in future development programs.

i. By no later than the end of 1st Quarter of FY 2023, FDA will publish a Federal Register Notice announcing the continuation of the paired meeting program, outlining program eligibility, and describing the proposal submission, selection process, and example topics that will advance the use of complex innovative designs and inform the development of a guidance document.

ii. FDA will select up to 8 proposals each year from proposals submitted to either CDER or CBER. The selections are expected to be made on a quarterly basis. Program selection will be prioritized based on trial design features and therapeutic areas of high unmet need.

iii. To promote innovation in this area, trial designs developed through the paired meeting program may be presented by FDA (e.g., in a guidance, at public workshops and conferences, on the Complex Innovative Design website) as case studies, including while the drug studied in the trial has not yet been approved by FDA. Before FDA grants the initial meeting, FDA and the sponsor will agree on the information that FDA may share publicly in these case studies. When feasible, FDA will notify a sponsor in advance when the sponsor's program is the planned focus of a public discussion. Participation in the paired meeting program, including such agreement on information disclosure, will be voluntary and at the discretion of the sponsor.

c. In order to encourage increased submissions by CBER-regulated sponsors to the complex innovative design (CID) paired meeting program, CBER staff will continue to engage in outreach to industry and other stakeholders. Such outreach will include providing information on the paired meeting program and its benefits, such as enhanced attention regarding CID proposals and advancing the leveraging and sharing of knowledge to support efficient product development; clarifying policies and procedures for submitting CID proposals for review; and presenting FDA's current thinking on CID-related technical topics.

d. Sponsors who do not participate in this paired meeting program will have an opportunity to interact with the Agency through traditional channels. This program will not affect FDA's existing procedures for providing advice on trial designs.

e. By the end of 2nd Quarter FY 2024, FDA will convene a public workshop to discuss aspects of complex adaptive, Bayesian, and other novel clinical trial designs. Discussion topics will include considerations for external data sources, Bayesian statistical methods, simulations, and clinical trial implementation (e.g. examples of defining and mitigating bias when using select trial design methods) and will be based on FDA accumulated experience both within and outside of the paired meeting program.

f. By the end of FY 2025, FDA will publish draft guidance on the Use of Bayesian Methodology in Clinical Trials of Drugs and Biologics. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

5. Enhancing Drug Development Tools Qualification Pathway for Biomarkers

To facilitate the enhancement of the drug development tools qualification pathway for biomarkers, FDA will conduct the following activities during PDUFA VII:

a. FDA will continue to retain and enhance the staff capacity to enhance biomarker qualification review by increasing base capacity. FDA will also pilot processes to engage external experts to support review of biomarker qualification submissions.

b. FDA will continue to publish information on its website regarding biomarker qualification submissions under section 507 of the FD&C Act, consistent with the requirements in section 507(c), and to update the website quarterly.

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

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) optimization of the Sentinel Initiative through a) maintenance of Sentinel Initiative capabilities and continued integration into FDA drug safety activities and b) enhancement of the analytic capabilities of the Sentinel Initiative to address questions of product safety and advance the understanding of how real-world evidence can be used for studying effectiveness.

1. Modernization and Improvement of REMS Assessments

FDA will use user fee funds to modernize and improve REMS assessments by incorporating REMS assessment planning into the design of REMS, clarifying its expectations regarding methods to evaluate the performance of REMS, increasing the efficiency of FDA's review of REMS assessment reports, and establishing FDA performance goals for review of REMS assessment methods and study protocols.

a. By March 31, 2024, update relevant guidances to incorporate REMS assessment planning into the design of the REMS by providing recommendations regarding: 1) linking the design with the assessments 2) ensuring sufficient and appropriate data collection, and 3) identifying key metrics for success (e.g., primary and secondary).

b. By March 31, 2024, FDA will issue new or update existing policies and procedures for reviewing methodological approaches and study protocols used to assess a REMS program.

c. Improve the efficiency of FDA's review of REMS assessment reports.

i. By March 31, 2024, FDA will issue new or update existing policies and procedures to systematically determine, as part of the review of REMS assessment reports, if modifications to the REMS or revisions to the REMS assessment plan are needed, including the timing of the REMS assessments and to determine whether the REMS is still necessary to ensure the benefits outweigh the risks of the drug.

ii. By March 31, 2026, FDA will develop draft guidance regarding the format and content of a REMS assessment report, including the type of data that can support elimination of a REMS. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months

after the close of the public comment period on the revised draft guidance.

d. Establish FDA review performance goals and provide feedback and comments on REMS methodological approaches and study protocols used to assess a REMS program for products within 90 days of receipt. FDA proposes the following staged implementation of review performance goals for review of methodological approaches and study protocols for REMS assessments in PDUFA VII:

i. FY 2024, review and notify sponsor with concurrence or comments within 90 days of receipt for 50% of REMS assessment methods and protocols

ii. FY 2025, review and notify sponsor with concurrence or comments within 90 days of receipt for 70% of REMS assessment methods and protocols

iii. FY 2026 and FY 2027, 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

The user fee funds initially provided in PDUFA VI to expand the Sentinel program will continue to systematically implement and integrate Sentinel and BEST (Biologics Effectiveness and Safety) Systems in FDA drug safety activities by sustaining the high quality and large quantity of data available, allowing continued application of advanced methods for determining when and how those data are utilized, and ensuring comprehensive training of review staff on the use of Sentinel and BEST. These capabilities will support the use of the Sentinel Initiative for regulatory decision making to address questions of product safety and advance our understanding of how real-world evidence can be used for studying effectiveness.

a. Maintenance of the Sentinel Initiative Capabilities and Continued Integration into FDA Drug Safety Activities

FDA will use user fee funds to maintain the quality and quantity of data available through the Sentinel Initiative (Sentinel and BEST), to maintain the processes and tools for determining when and how those data are utilized, and to support comprehensive training of review staff on the use of Sentinel.

i. FDA will maintain the Sentinel's sources of data and core capabilities for the safety surveillance of drugs and biologics, including the multisite ARIA system.

ii. FDA will continue its communication with sponsors and the public regarding general methodologies for Sentinel queries, including what the Agency has learned regarding the most appropriate ways to query and use Sentinel data.

iii. By the end of FY 2025, FDA will publish on its website an update on facilitation of public and sponsor access to Sentinel's distributed data network to conduct safety surveillance.

iv. FDA will continue to post study results, study parameters and analysis code online and maintain a strong Sentinel web presence to host this information.

v. FDA will continue to maintain a comprehensive FDA Sentinel training program for all relevant staff (e.g., epidemiologists, statisticians, project managers, medical officers, clinical analysts, and other review team members) to ensure that staff have a working knowledge of Sentinel, can identify when Sentinel can inform important regulatory questions and decisions, and are able to consistently participate in use of Sentinel to evaluate safety issues.

vi. By the end of FY 2025, FDA will analyze, and report on the use of Sentinel for regulatory purposes, e.g., in the contexts of labeling changes, PMRs, or PMCs.

vii. For FY 2023–2027, FDA will report its obligations for updated PDUFA VI commitments for PDUFA VII Sentinel Initiative annually in the PDUFA Financial Report. This reporting will provide detail for spending categories (e.g., data infrastructure, analytical capabilities, safety issue analyses, dissemination of relevant product and safety information, and Sentinel system development).

b. Enhancement of the Analytic Capabilities of the Sentinel Initiative to Address Questions of Product Safety and Advance the Understanding of How Real-World Evidence Can Be Used for Studying Effectiveness

FDA will use user fee funds to advance the analytic capabilities of the Sentinel Initiative by i) developing a consistent approach to post-market requirements and commitments during NDA and BLA review related to assessing the outcomes of pregnancies in women exposed to drugs and biological products and clarifying the optimal use and value of pregnancy registries and electronic healthcare data for assessing pregnancy safety and ii) supporting the use of real-world evidence to address questions of product safety and advancing our understanding of how real-world evidence may be used for studying effectiveness.

i. Pregnancy Safety

The goal of pregnancy safety post-market requirements and commitments studies is to inform labeling on the safety of use in pregnancy and to detect or evaluate safety signals in a timely manner.

(1) FDA will develop a framework describing how data from different types of post-market pregnancy safety studies might optimally be used, incorporating knowledge of how different types of postmarket studies have been used by FDA and industry and identifying gaps in knowledge needed to be filled by demonstration projects. The framework would consider factors such as, but not limited to, purpose of study, types of post-market studies, anticipated exposure in females of reproductive potential (FRP) and pregnant women, potential toxicity of the drug and proposed risk mitigation, benefits of the drug, and magnitude and type of risk to be detected. The framework would specifically address the use of pregnancy registries and electronic healthcare data sources including Sentinel, with a goal of ensuring the most efficient means of obtaining highest quality safety data available.

(a) FDA will review published literature and conduct a review of types of post-market pregnancy data that have been included in pregnancy labeling.

(b) By September 30, 2023, FDA will hold a public workshop on post-market safety studies in pregnant women to facilitate determination of the ideal post-market study design(s), including industry experience and use of Sentinel Initiative and other real-world data resources.

(c) By September 30, 2024, FDA will publish a workshop report describing the proposed framework.

(2) Incorporating feedback from (1), conduct 5 demonstration projects to address gaps in knowledge about performance characteristics of different study designs. FDA will initiate the following demonstration projects which may be modified as needed, before September 30, 2024:

(a) Assess the performance of pregnancy registries versus electronic healthcare database studies to detect a signal when the exposure to medication in pregnancy is relatively common.

(b) Assess the performance of single arm safety studies versus signal identification methods using electronic healthcare data to detect a signal when the exposure to medication in pregnancy is anticipated to be low.

(c) Assess the performance of pregnancy registries versus electronic healthcare database studies to evaluate a signal when the exposure to medication in pregnancy is relatively common.

(d) Assess the performance of major congenital malformations

(MCM) as a composite outcome in signal detection and evaluation when there is true risk for some but not all specific malformations.

(e) Assess the performance of an algorithm using electronic health record (EHR) and claims-linked healthcare data for a pregnancy-related outcome, or composite of outcomes (e.g., spontaneous abortion, stillbirth, congenital malformations), after use of vaccines in pregnant women. The parameters of the pregnancy-outcome algorithm will be developed to have general usability with therapeutic products.

(3) By September 30, 2027, based on the results of demonstration projects in (2) update the proposed framework and develop a guidance or MAPP/SOPP as appropriate to implement a standardized process for determining necessity and type of pregnancy post-marketing studies including PMRs.

ii. Use of Real-World Evidence—Negative Controls

FDA is building Sentinel/BEST methodology to improve understanding of robustness evaluations used to address the consistency of RWE with respect to study design, analysis, or variable measurement. FDA will develop new methods to support causal inference in Sentinel/BEST that could address product safety questions and advance our understanding of how RWE may be used for studying effectiveness.

(1) By September 30, 2023, FDA will hold a public workshop on use of negative controls for assessing the validity of non-interventional studies of treatment and the proposed Sentinel Initiative projects.

(2) FDA will initiate two methods development projects by September 30, 2024 to 1) develop an empirical method to automate the negative control identification process in Sentinel and integrate it into the Sentinel System tools; and 2) develop a method to use a double negative control adjustment to reduce unmeasured confounding in studying effectiveness of vaccines.

(3) By September 30, 2027, FDA will publish a report on the results of the development projects.

N. Enhancements Related to Product Quality Reviews, Chemistry, Manufacturing, and Controls Approaches, and Advancing the Utilization of Innovative Manufacturing Technologies

To ensure new and innovative products are developed and available to patients in a timely manner, FDA and industry will focus on enhancing communications during drug development and application review, enhancing support for CMC development and facilitating the CMC readiness of products with accelerated clinical development timelines, and advancing the implementation of innovative manufacturing technologies.

1. Enhancing Communication Between FDA and Sponsors During Application Review

To promote an efficient and effective application review process, FDA will conduct the following activities during PDUFA VII to enhance communication between the FDA review teams and sponsors:

a. The four essential components of CMC information requests (referred to as Four-Part Harmony) are intended to ensure that the FDA requests information that is appropriate to address the question or issue, in an efficient manner, and at the appropriate timepoint within the review cycle or product lifecycle, as applicable. Use of Four-Part Harmony includes acknowledging what was

provided and where (e.g., modules, page numbers, as applicable), identifying the issue or deficiency, clearly identifying the information needed to achieve resolution and make a regulatory decision, and identifying specific references or other information to support FDA's request. These four essential components of Four-Part Harmony are:

i. What was provided
ii.What is the issue or deficiency
iii. What is needed
v. Why it is needed

By the end of FY 2023, to promote FDA reviewers' use of Four-Part Harmony, FDA will update and conduct training on CDER MAPP 5016.8, ''Communication Guidelines for Quality-Related Information Request and Deficiencies'' and CBER SOPP 8401.1, ''Issuance of and Review of Responses to Information Request Communications to Pending Applications'' describing the guidelines for the content of information requests, based on the principles of Four-Part Harmony.

b. By the end of FY 2023, FDA will update and conduct training on CMC assessment processes associated with mid-cycle and late-cycle review meetings with the goal of ensuring that mid-cycle and late-cycle meeting expectations are met, including communicating the status of the NDA and BLA CMC assessment and any identified issues that would preclude approval.

c. FDA will contract with an independent third party to assess current practices of FDA (CDER and CBER) and sponsors in communicating through product quality information requests (IRs) during application review, not including supplements.

The assessment will focus on the application of Four-Part Harmony as described in the MAPPs and SOPPs (e.g., did FDA state why the information is needed for the review of the application) as well as seek to identify trends across IRs. The statement of work for this effort will be published for public comment prior to beginning the assessment. The third party will be expected to separately engage both FDA staff and individual sponsors through contractor-led interviews as part of the assessment. The contractor-led interviews will be designed to provide feedback from individual sponsors on the effectiveness of Four-Part Harmony. Due to the significant volume of IRs in a given year, the assessment will be based on a subset of drug and biologic applications, not including supplements, balanced across CDER and CBER, proportional to the number of applications received by each Center. The third party will identify best practices and areas for improvement in communication between FDA review staff and sponsors through IRs. FDA will publish the final report of the assessment on FDA's website no later than June 30, 2025, for public comment.

2. Enhancing Inspection Communication for Applications, not Including Supplements

FDA and industry believe enhanced communication between review teams and 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.

3. Alternative Tools to Assess Manufacturing Facilities Named in Pending Applications

During the COVID–19 public health emergency, the FDA expanded its use of alternate tools for assessing facilities named in applications, including exercising its authority to request records and other information in advance of or in lieu of an inspection, granted per section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 374(a)). Where appropriate, the agency also increased the use of information, including inspection reports, shared by trusted foreign regulatory partners through mutual recognition agreements and other confidentiality agreements. As FDA continues to gain experience and lessons learned from the use of these tools, FDA will communicate its thinking on the use of such methods beyond the pandemic.

By September 30, 2023, FDA will issue draft guidance on the use of alternative tools to assess manufacturing facilities named in pending applications (e.g., requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, requesting records and other information directly from facilities and other inspected entities, and, as appropriate, utilizing new or existing technology platforms to assess manufacturing facilities). The guidance will incorporate best practices, including those in existing published documents, from the use of such tools during the COVID–19 pandemic. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

4. Facilitating Chemistry, Manufacturing, and Controls Readiness for Products with Accelerated Clinical Development

Development programs for CDER- and CBER-regulated drugs and biologics intended to diagnose, treat, or prevent a serious disease or condition where there is an unmet medical need may have accelerated clinical development timelines. Products with accelerated clinical development activities often face challenges in expediting CMC development activities to align with the accelerated clinical timelines. Overcoming these CMC challenges often requires additional interaction with FDA during product development and the use of science-and risk-based regulatory approaches so that the clinical benefits of earlier patient access to these products can be realized.

a. MAPP: By December 31, 2022, FDA will issue a new MAPP on approaches to address CMC challenges for CDER-regulated products (drugs, biologics) with accelerated clinical development timelines (e.g., products used to diagnose, treat, or prevent a serious disease or condition where there is unmet medical need). To address the CMC challenges, the MAPP will describe early engagement with sponsors of such products and the different science-and risk-based approaches, including those described in the FDA Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics, that may be warranted and utilized in CMC development based upon the anticipated clinical benefit of earlier patient access to the product. The MAPP will incorporate modern pharmaceutical principles as well as modern regulatory tools, such as those detailed in ICH Q12.

b. Pilot: Starting in FY 2023, FDA (CDER and CBER) will conduct a CMC Development and Readiness Pilot (CDRP) to facilitate the expedited CMC development of products under an IND application, where warranted, based upon the anticipated clinical benefit of earlier patient access to the products. The goal of the Pilot will be to facilitate CMC readiness for CBER- and CDER-regulated products with accelerated clinical development timelines. Due to the differences in product complexity between CBER- and CDER-regulated products, Pilot selection criteria may differ between the Centers. In order to accelerate CMC development and facilitate CMC readiness, the Pilot will incorporate, as applicable, contemporary learnings and the use of science- and risk-based approaches and submission strategies, such as those described in the FDA Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

For sponsors participating in the CMC Development and Readiness Pilot, FDA will provide specific CMC advice during product development by providing two additional CMC-focused Type B meetings and an additional limited number of CMC-focused discussions based on readiness and defined CMC milestones. The increased communication between FDA review staff and applicants is intended to ensure a mutual understanding of what activities must be completed, and what information should be provided at the appropriate timepoint (i.e., at the time of NDA or BLA submission, prior to the end of the review cycle, or post-approval), to ensure CMC readiness of the product.

i. By December 31, 2022, FDA will publish a Federal Register Notice (FRN) announcing the Pilot and outlining the eligibility criteria and process for submitting a request to participate in the Pilot. For CDER, the eligibility criteria will focus on the selection of products with accelerated clinical development timelines that could expand or enhance the approaches in the CDER MAPP described above. For CBER, the eligibility criteria will include considerations for products with accelerated clinical development timelines (e.g., vaccines and cell and gene therapies).

The FRN will give more specifics on products to be included in the Pilot and will consider Industry's interest in CBER-regulated products such as cell and gene therapies. FDA will select between 8–10 proposals per fiscal year over a 4–year period.

ii. To promote innovation and understanding in this area, lessons learned through the Pilot may be presented by FDA (e.g., in a public workshop) as case studies, including when the product studied in the Pilot has not yet been approved by FDA. To be eligible for the Pilot, the sponsor and FDA will reach an agreement on the information to be publicly disclosed. When feasible, FDA will notify a sponsor in advance when the sponsor's program is the planned focus of a public discussion. Participation in the pilot program, including such agreement on information disclosure, will be voluntary and at the discretion of the sponsor.

iii. Sponsors who do not participate in the Pilot will have an opportunity to interact with the Agency through existing channels.

c. Public Workshop: By July 31, 2025, FDA will conduct a public workshop, potentially through a qualified third party, focused on CMC aspects of expedited development including case studies, lessons learned, and stakeholder input regarding the CMC Development and Readiness Pilot. The workshop will solicit and include industry and public feedback.

Topics for the workshop will include, but are not limited to, the use of science and risk-based approaches and submission strategies to accelerate CMC development, including predictive stability modeling, risk-based approaches to product specification setting,

and alternate process validation approaches, as well as experiences related to quality by design and platform technologies.

d. Strategy Document: Following the close of the public comment period for the public workshop, and no later than April 30, 2026, FDA will issue a strategy document outlining the Agency's plans, including proposed timeframes, to develop or revise, as appropriate, relevant MAPPs or SOPPs, and other applicable documents (e.g., guidance and process documents) to incorporate lessons learned from the Agency's experiences with the CMC Development and Readiness Pilot and other submissions for products with accelerated clinical development timelines, as well as industry and public input, including feedback from the public workshop.

5. Advancing Utilization and Implementation of Innovative Manufacturing

By the end of FY 2023, FDA will conduct a public workshop on the utilization of innovative manufacturing technologies for CDER- and CBER-regulated products, including barriers to their adoption and submission strategies. The workshop will solicit and include industry and public feedback.

Topics for the workshop will include but are not limited to:

a. Best practices and lessons learned from both the CDER Emerging Technology Team and CBER Advanced Technology Team programs from both industry and regulatory perspectives;

b. Case studies from previous innovative technology submissions presented by sponsors;

c. Barriers (technical, regulatory, etc.) to the adoption of innovative manufacturing technologies;

d. Regulatory strategies for the adoption of advanced manufacturing technologies, including, but not limited to, submission strategies for the implementation of certain innovative technologies across multiple commercial products and/or multiple manufacturing sites; and

e. Science- and risk-based approaches for developing and assessing innovative technologies across platform products and sites to streamline adoption.

Following the close of the public comment period for the public workshop, and no later than September 30, 2024, FDA will issue a draft strategy document for public comment that outlines the specific actions the agency will take over the course of PDUFA VII to facilitate the utilization of innovative manufacturing technologies, including addressing barriers to their adoption. The actions described in the draft strategy document will be based on lessons learned from the Agency's experiences with submissions involving advanced manufacturing technologies as well as feedback from the workshop and other public input. The strategy document may include updating or creating new procedures, MAPPs, SOPPs, guidances, and scientific/other relevant programs related to the topics discussed in the workshop. The strategy document will also include proposed timeframes for the specific actions outlined in the document.

FDA will consider public input and finalize the strategy document within 9 months after the close of the public comment period on the draft strategy document.

O. Enhancing CBER's Capacity to Support Development, Review, and Approval of Cell and Gene Therapy Products

To ensure that new and innovative cell and gene therapy products are developed and available to patients in a timely manner, FDA will build on the success of the Cell and Gene Therapy Program (CGTP) in CBER to further support and advance a balanced approach to product development and regulation. To this end, FDA will substantially strengthen staff capacity and capability in order to meet the increasing challenges and demands in this growing field. Increasing staff capacity will overcome existing resource limitations, allowing staff to spend additional time on meetings and submission reviews including those with breakthrough or regenerative medicine advanced therapy designations, expand stakeholder outreach, invest in new policy and guidance, and facilitate development and use of regulatory tools and scientific technologies.

The CGTP will be augmented with additional resources to sustain and expand the program. Staff will be hired for direct review activities, indirect activities (e.g., policy, external outreach, postmarket safety), and supporting activities in the CGTP, with a focus on hiring staff with technical, scientific, clinical, or other specialized expertise necessary to understand and advance cell and gene therapies. Recruiting and hiring of staff will be actively pursued as a CBER priority and be facilitated by support staff whose dedicated focus will be attracting and retaining talent for the CGTP. CBER recognizes the importance of integration of new staff into the CGTP and will effectively facilitate growth in staffing using external consultants when appropriate. For PDUFA VII, resources will also support onboarding and integration of new staff, regulatory support and outreach (e.g., webinars, recorded training) to facilitate industry and stakeholder education and interaction.

CBER will continue to maintain a highly trained and experienced CGTP staff, with an emphasis on remaining current in regulatory science, and the latest scientific, manufacturing, and clinical advances. The current staff training will be reviewed, with input from external consultants, and modified as needed to accommodate and facilitate training of new staff and maintain the competency of existing staff.

CBER will continue to organize and manage the CGTP for optimal performance, leveraging and implementing best practices from relevant sources. The current CGTP organization will be evaluated, with input from external consultants, to determine the optimal organization to effectively integrate new staff and facilitate operations and customer service. As part of CBER's modernization program, CBER will evaluate, streamline, and harmonize CGTP procedures, processes, and interactions to facilitate communications, enhance regulatory consistency and review standards, reduce regulatory burden, optimize operational efficiency, and update relevant SOPPS and documents as needed. Change management will be tailored to ensure success of organizational changes and business modernization.

The CGTP staff will enhance communications with stakeholders, on an individual and collective level, by refining and improving best practices for communication, through public meetings and workshops, and issuance of guidance, updating relevant SOPPS, and other mechanisms. CBER will continue to issue new guidance on current cell and gene therapy topics and update existing guidance to be current with evolving science and approaches. Staff will increase awareness of FDA's regulatory programs through on-demand training (e.g., recorded webcast), to facilitate navigation by industry through the phases of product development and approval. CGTP staff will continue to engage in outreach to industry, patient groups, and other stakeholders in several areas soliciting views on specific topics and proposals.

Staff will continue to participate in external collaborations, including public-private partnerships and international organizations in a variety of areas, including development of tools (e.g., standards), technologies, and approaches that support development of cell and gene therapies. Interactions will also focus on advancing manufacturing and testing, including facilitating implementation of new technologies. With stakeholders, staff will continue discussing 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 with specific consideration and attention to rare and ultra-rare diseases.

To advance the field and support the next generation of cell and gene therapy products, CBER will conduct the following activities during PDUFA VII.

1. Patient Focused Drug Development

a. By the end of FY 2023, FDA will convene a public patient focused drug development meeting with key stakeholders, including patients and patient advocacy organizations, to better understand patient perspectives on gene therapy products, including cell-mediated gene therapy. This meeting should address, among other things, the patient and caregiver's level of understanding and expectations regarding the benefits and risks of these therapies, and their involvement in clinical study design and execution. Within 6 months of the public meeting, FDA will issue a report summarizing the views expressed at the meeting including:

i. Analysis of current tools or methods used to capture patient experience data, and/or patient involvement in clinical studies, including identification of existing challenges and gaps;

ii. Whether there is a need for the community to develop specific tools or methods to capture patient experience data, and/or patient involvement in clinical studies that are unique to these products, and if so, suggestions for community engagement strategies; and

iii. Approaches to leveraging existing tools or methods to capture patient experience and patient preference data that are unique to these products;

2. Novel Approaches to Development of Cell and Gene Therapy

a. FDA will continue to work with stakeholders including public-private partnerships to seek public input 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, and to facilitate development and approval for cell and gene therapies, including but not limited to, individualized therapies, rare disease and therapies for small patient populations.

b. By the end of FY 2025, FDA will issue a draft guidance on the evaluation of efficacy in small patient populations using novel trial designs and statistical methods, and how these concepts can be applied to more common diseases. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

c. In order to promote development of cell and gene therapy products, FDA will issue a Questions and Answers draft guidance by the end of FY 2024 based on frequently asked questions, and commonly faced-issues identified by sponsors or by public-private partnerships. FDA will work towards the goal of publishing final guidance within 18 months

after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

d. By the end of FY 2024, FDA will convene a public meeting to solicit input on methods and approaches (e.g., use of RWE, registries) for capturing post-approval safety and efficacy data for cell and gene therapy products. Within 6 months of the public meeting, FDA will issue a summary report or a transcript of the meeting. Input from this meeting will be used to inform development of a draft guidance on this topic. FDA will issue a draft guidance on this topic by the end of FY 2025. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

3. Expedited Programs for the Development of Regenerative Medicine Therapies:

a. By the end of FY 2025, FDA will update the Guidance for Industry: Expedited Programs for Regenerative Medicine Therapies for Serious Conditions. Updates will include, for example, additional thinking on post-approval requirements, including the use of real-world evidence to confirm clinical benefit, for products approved under accelerated approval, as well as for safety monitoring and long-term follow-up. Updates will also include additional thinking on approaches and processes relating to CMC including considerations regarding CMC readiness to take advantage of the expedited programs. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

4. Leveraging Knowledge

a. FDA will continue to work with organizations, including public-private partnerships, that foster development and accessibility of non-proprietary knowledge (e.g., standards), manufacturing advances, and manufacturing components for use in cell and gene therapy products. FDA will continue to participate in international organizations sharing knowledge and perspective to harmonize cell and gene therapy guidance as appropriate.

b. By the end of FY 2025, FDA will convene a public meeting to solicit the perspective of cell and gene therapy manufacturers on how individual sponsors might leverage internal prior knowledge and public knowledge, including Chemistry, Manufacturing, and Controls, non-clinical, and clinical knowledge, across therapeutic contexts in order to facilitate product development and application review. Input from this meeting will be used to inform development of a draft guidance on this topic that FDA will issue by the end of FY 2026. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

P. Supporting Review of New Allergenic Extract Products

FDA will use fee revenues to support the review of new allergenic extract products that have been incorporated in the PDUFA program by PDUFA VII. Allergenic extract products licensed after October 1, 2022 will generally be included in user fees. 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 will remain excluded from PDUFA. All performance goals, procedures, and commitments in this letter apply to the allergenic products included in the PDUFA program under PDUFA VII.

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 included in PDUFA VI and continue activities in PDUFA VII to ensure optimal use of user fee resources and the alignment of staff to workload through the continued maturation and assessment of the Agency's resource capacity planning capability. 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 activities to mature the Agency's resource capacity planning function, including utilization of modernized time reporting, to support enhanced management of PDUFA resources in PDUFA VII and help ensure alignment of user fee resources to staff workload.

1. Resource Capacity Planning Implementation

a. By the end of the 2nd quarter of FY 2023, FDA will publish an implementation plan that will describe how resource capacity planning and time reporting will continue to be implemented during PDUFA VII. This implementation plan will address topics relevant to the maturation of resource capacity planning, including, but not limited to, detailing FDA's approach to:

i. The continued implementation of the Agency's resource capacity planning capability, including:

1) The continual improvement of the Capacity Planning Adjustment (CPA); and

2) The continual improvement of time reporting and its utilization in the CPA.

ii. The integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes.

b. FDA will provide annual updates on the FDA website on the Agency's progress relative to activities detailed in this implementation plan by the end of the 2nd quarter of each subsequent fiscal year.

c. FDA will document in the annual PDUFA Financial Report how the CPA fee revenues are being utilized.

2. Resource Capacity Planning Assessment

By the end of FY 2025, an independent contractor will complete and publish an evaluation of the resource capacity planning capability. This will include an assessment of the following topics:

a. The ability of the CPA to forecast resource needs for the PDUFA program, including an assessment of the scope of the workload drivers in the CPA and their ability to represent the overall workload of the PDUFA program;

b. Opportunities for the enhancement of time reporting toward informing resource needs; and

c. The integration and utilization of resource capacity planning information within resource and operational decision-making processes of the PDUFA program.

The contractor will provide options and recommendations in the evaluation regarding the continued enhancement of the above topics as warranted. The evaluation findings and any related recommendations will be discussed at the FY 2026 PDUFA 5-year financial plan public meeting. After review of the findings and recommendations of the evaluation, FDA will, as appropriate, continue improving the resource capacity planning capability and the CPA.

B. Financial Transparency

1. FDA will publish a PDUFA 5-year financial plan no later than the end of the 2nd quarter of FY 2023. The plan shall recognize that the retention of the strategic hiring and retention adjustment required by section 736(b)(1)(C) of the FD&C Act is subject to renegotiation under a subsequent reauthorization of PDUFA. FDA will publish updates to the 5-year plan no later than the end of the 2nd quarter of each subsequent fiscal year. The annual updates will include the following topics:

a. The changes in the personnel compensation and benefit costs for the process for the review of human drug applications that exceed the amounts provided by the personnel compensation and benefit costs portion of the inflation adjustment; and

b. FDA's plan for managing costs related to strategic hiring and retention after the adjustment required by section 736(b)(1)(C) of the FD&C Act expires at the end of fiscal year 2027, given this adjustment is not intended to be reauthorized in a subsequent reauthorization of PDUFA.

2. FDA will convene a public meeting no later than the end of the 3rd quarter of each fiscal year to discuss the PDUFA 5-year financial plan and the Agency's progress in implementing resource capacity planning, including the continual improvement of the CPA and time reporting, and the integration of resource capacity planning in resource and operational decision-making processes.

3. FDA will include in the annual PDUFA Financial Report 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.

III. IMPROVING FDA HIRING AND RETENTION OF REVIEW STAFF

Enhancements to the human drug review program require that FDA hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of human drug applications. During PDUFA VII, FDA will commit to do the following:

A. Set Clear Goals for Human Drug Review Program Hiring

1. FDA will establish priorities for management of the metric goals for targeted hires within the human drug review program staff

for the years of PDUFA VII. These goals for targeted hires are summarized in Table 6 below:

TABLE 6

	FY 2023	FY 2024	FY 2025	FY 2026	FY 2027
CBER	132	48	29	15	4
CDER	77	31	15	0	0
Other FDA	1	0	0	0	0
Total FTE	210	79	44	15	4

2. FDA will confirm progress in the hiring of PDUFA VI new staff. FDA will also report on progress against the hiring goals for FY 2023–2027 on a quarterly basis posting updates to the FDA website PDUFA Performance webpage.

B. Assessment of Hiring and Retention

The Directors of CDER and CBER will utilize a qualified, independent contractor with expertise in assessing HR operations to conduct a targeted assessment of the hiring and retention of staff for the human drug review program. The contractor will assess the factors that contribute to HR successes and challenges, including factors outside of FDA's control. The assessment will build upon the findings of previous evaluations conducted under PDUFA VI with a focus on the changes and adjustments that have improved FDA's hiring and retention outcomes and which challenges remain. In addition to evaluating the outcomes of various hiring changes, the assessment will include metrics related to recruiting and retention in the human drug review program, including, but not limited to, specific targeted scientific disciplines, attrition, and utilization of pay authorities. The report will include the contractor's findings and recommendations on further enhancements to hiring and retention of staff for the human drug review program, if warranted.

The assessment will be published on FDA's website no later than the June 30th, 2025 for public comment. FDA will also hold a public meeting no later than the September 30th, 2025 to discuss the report, its findings, and the Agency's specific plans to address the report recommendations.

IV. INFORMATION TECHNOLOGY AND BIOINFORMATICS GOALS

A. Enhancing Transparency and Leveraging Modern Technology

Under PDUFA VII, FDA will:

1. Enhance Transparency

FDA will further enhance transparency of its IT activities and modernization plans, as well as continue to ensure the usability and improvement of the electronic submissions gateway (ESG):

a. Quarterly, FDA and industry will jointly plan and conduct meetings on challenges, emerging needs, and progress on initiatives relevant to PDUFA, including continued sustainability of initiatives after completion in PDUFA VII, progress or activities on harmonization and convergence, where appropriate, across Center systems for streamlined compatibility, interoperability, and extensibility. Agendas and meeting materials will be shared prior to each meeting.

b. Annually, appropriate FDA and industry IT leadership (e.g., enterprise IT leadership, Center IT leadership) will participate in a review of PDUFA IT initiatives and provide an opportunity for industry input.

c. FDA will engage industry to provide feedback and/or participate in pilot testing in advance of implementing significant changes that impact industry's interaction with the enterprise-wide systems.

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

2. Develop Data and Technology Modernization Strategy

FDA will progress a Data and Technology Modernization Strategy (''Strategy'') that provides FDA's strategic direction for current and future state data-driven regulatory initiatives.

a. No later than Q4 FY 2023, FDA will establish a Data and Technology Modernization Strategy that reflects the vision in FDA's Technology and Data Modernization Action Plans, including:

i. outlining key areas of focus and approach including leveraging cloud technologies to support Applicant-FDA regulatory interaction;

ii. articulating enterprise-wide approaches for both technology and data governance; and

iii. aligning strategic initiatives in support of PDUFA review goals, drawing a line of sight between initiatives and the enterprise strategy (i.e. the agency-wide strategy also supporting components outside PDUFA).

b. The Strategy will be shared and annually updated to reflect progress and any needed adjustments. Milestones and metrics for PDUFA initiatives will be included in the updates.

3. Promote Convergence

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

a. FDA will seek to adopt international standards where feasible and appropriate, giving considerations to cybersecurity risk, international commitments, legal constraints, and other relevant factors.

4. Accelerate CBER Modernization

During PDUFA VII, CBER will retire its older IT systems and capabilities, leverage capabilities in other Centers where feasible, and utilize new data management tools and technologies in line with Agency strategic plans and effective use of resources.

In coordination with CDER and CDRH, CBER will accelerate its data and IT modernization in order to leverage or develop state-of the art IT technology to provide cloud-based, agile, and stable integrated platforms, to streamline and improve its ability to perform complex reviews, access, utilize and protect data, and redirect IT spending from maintenance of older IT systems to improving the reviewer experience. Modernization efforts will enable new capabilities such as knowledge management, data and analytic reporting, decision tools, and, workflow and workload management to be developed sooner. CBER will share its experience and new capabilities with other Centers.

b. By the end of Q4 FY 2022, CBER will have established a multi-year modernization roadmap, including concrete implementation phases and milestones with defined success and performance criteria and anticipated costs.

i. Criteria may include, for example, retiring a minimum 25% of CBER legacy systems and capabilities by the end of PDUFA VII; leveraging existing adverse events reporting capabilities for CBER adverse event reporting; transitioning regulatory data and analytics to a new shared environment; using a new electronic review management tool and knowledge management system.

ii. These and other modernization efforts will allow for measurable improved review and internal management of novel and scientifically complex PDUFA biologics, leading to enhanced review efficiency, effectiveness and quality.

iii. Modernization outcomes will facilitate external interactions with developers, manufacturers, and other stakeholders—resulting in faster information exchange, data analysis, and dissemination of safety information; and better consistency of advice and decisions to guide and foster product development and review.

c. Annually and at key milestones, CBER will share its roadmap, provide updates on its progress including successes, issues, performance metrics, accomplishments and any issues or necessary adjustments to accommodate unexpected events (e.g., contracting, delays outside of CBER control) or reasonable deviations from its modernization roadmap. This information will be shared at regularly scheduled FDA-industry meetings.

d. In order to ensure successful modernization, CBER maintains active management and oversight of its IT and Data projects through a structured system of controls that covers all phases of projects. CBER will not progress to the next phase of implementation for an IT modernization project without successful completion of the previous phase.

e. CBER will scope and plan its IT modernization activities to conclude by the end of FY 2027 with no expectation of continued additional direct costs funding to support the effort beyond PDUFA VII.

5. Monitor and Modernize ESG

FDA will continue to ensure the usability and improvement of the ESG.

a. Annually, FDA will provide on the ESG website historic and current metrics on ESG performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.

FDA will advance the ESG cloud-based modernization with an improved architecture that supports greatly expanding data submission bandwidth and storage, while continuing to ensure its stable operation.

a. By the end of FY 2025, FDA will complete ESG transition to the cloud, including set-up and integration of an enterprise Identity and Access Management solution that will streamline applicant access to FDA resources.

b. Annually, FDA will share progress against the implementation project plan.

c. FDA will engage industry to provide feedback and/or participate in pilot testing in advance of implementing significant changes that impact industry's interaction with the enterprise-wide systems.

6. Leverage Cloud Technology to Progress Regulatory Digital Transformation

Cloud and cloud-based technology offer significant advantages over traditional on-premise data repositories and analytics. Combined with interoperable information exchange mechanisms, these advantages open a host of new opportunities to explore, promote and implement innovation in the drug development and regulatory review process.

The outcomes of demonstration projects in PDUFA VII will be the building blocks, informing and positioning FDA and regulated industry to take best advantage of third-party hosted capabilities in conjunction with their own infrastructure, as well as investigating the potential for such capabilities to be jointly leveraged by other regulatory authorities and applicants.

a. FDA will engage with external parties to develop and test reusable and portable core capabilities that can be supported both with FDA's environment and in trusted third-party environments. This engagement will be through mechanisms such as, but not limited to, cooperative agreements, contracts, Cooperative Research and Development Agreements (CRADAs) and public-private partnerships.

b. By the end of Q3 FY 2023, FDA will assess challenges or barriers in FDA's adoption of cloud-based technologies in applicant-regulator interactions and within 6 months will publish the findings of this assessment.

c. In FY 2023, FDA, in consultation with industry, will prioritize and initiate the first of at least 3 demonstration projects to explore application of cloud-based technologies to streamline, improve and enable a variety of applicant-regulator interactions.

i. In support of the use of DHT-derived data in applications, FDA will enhance its capability to effectively receive, aggregate, store, and process large volumes of static or continuously updated DHT-derived data captured as part of a clinical trial.

ii. Projects will demonstrate applications of cloud technology to applicant-regulator interactions and secure shared environments for specific regulatory activities (e.g., support labeling negotiations between FDA and applicants, develop a standard protocol template to accelerate review and provide usable archive, improve statistical analysis plan between FDA and applicants).

iii. Projects will develop increasingly rich and flexible technical capabilities that can be leveraged for multiple purposes by regulators and industry, either internally within a regulator's or industry's environment, or through a trusted third-party, thus promoting convergence through common components such as Cloud-hosted Individualized Secure Collaboration Hubs (ISCH) which provide secure and effective environments for various cloud-based collaboration initiatives;

1) An example might be to utilize an ISCH for applicant-regulator label negotiations; another might be to hold continuously updated DHT-derived data for analysis.

d. Within 6 months of completion of a demonstration project, a summary of outcomes and next steps will be compiled and shared with industry at the regularly scheduled FDA-industry meetings. A description of the project and summary of outcomes will be posted on the FDA website.

e. FDA will engage industry to provide feedback and/or participate in testing in advance of implementing significant changes that impact industry's interaction with the enterprise-wide systems.

i. FDA will review progress and plans at quarterly meetings with industry.

f. Demonstration projects and associated capabilities development will be completed by the end of FY 2027 with no expectation of additional funding for those activities beyond PDUFA VII.

7. Provide Bioinformatics IT Support

CDER and CBER are seeing increasing volume and diversity of bioinformatics and computational biology information and data, such as Next Generation Sequencing, in sponsor-regulator interactions. Bioinformaticists play an essential and expanding role in new drug and biologic application reviews, providing in-depth independent analysis of submitted data to support review decisions in close coordination with clinical and product experts. To be effective entails appropriate IT support.

a. FDA will 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.

b. Outcomes will be shared at regularly scheduled FDA-industry meetings.

B. Expanding and Enhancing Bioinformatics Support

Bioinformatics and computational biology are increasingly being used to assess product quality, safety and efficacy and facilitate the development, characterization and manufacture of human drugs and biologics. Recognizing the substantial increase in the volume and diversity of bioinformatics and computational biology information and data, such as Next Generation Sequencing, in regulatory submissions, FDA will develop additional expertise and staff capacity in both CDER and CBER to efficiently review and provide technical and timely feedback on information and accompanying data in submissions and meet performance goals, especially for those submitted early in development. FDA will hire technical expertise necessary to assess the approaches and evaluate data as appropriate, validating the results and/or analytic process using existing tools or through independent analysis when necessary. Staff with specialized expertise in specific product/therapeutic areas will also be developed to facilitate translation of bioinformatic information to subject matter review experts. FDA will also assess and strengthen its computational infrastructure to support and advance its informatics platforms, allowing FDA to remain current with the most recent technology in the field. To facilitate submission and review of bioinformatics and computational biology information, FDA will continue to develop data standards and revise guidance or issue draft guidance on this topic including how to submit, and format submissions, and technical validation criteria. FDA will work globally to advance harmonization of these standards and methodologies.

C. Enhancing use of Digital Health Technologies to Support Drug Development and Review

A Digital Health Technology (DHT) in the context of this commitment may be considered as a system that uses computing platforms, connectivity, software, and sensors for healthcare and related uses. These technologies may span a wide range of uses, from applications in general wellness to applications as a medical device to applications generating data that may be used in the evaluation of drug or biologic products.

DHTs can allow for remote data acquisition from patients and clinical trial participants to measure a wide range of activities, behaviors, and functioning in real life settings that can inform important clinical endpoints. DHTs may include wearable, implantable, ingestible, and environmental sensors or software applications on mobile devices, among other approaches. The use of DHTs can support and enable the conduct of decentralized clinical trials (DCTs), the clinical investigations in which some or all trial-related procedures and data acquisition take place at locations remote from the investigator.

While the biomedical field has experienced rapid development and implementation of DHTs, FDA has limited experience evaluating novel DHT-based measurements in human drug development. FDA recognizes the potential for DHTs to provide scientific and practical advantages in supporting the assessment of patients by generating information outside of the traditional clinic visit and needs to build capacity and expertise to advise the biopharmaceutical industry in their development and implementation and to evaluate DHT outputs including the impact of regulatory initiatives (or regulatory science). To support new drug registration, label expansion, and safety monitoring, DHT-based data need to be fit for the intended purpose. Toward these ends, FDA will do the following:

1. By the end of Q2 FY 2023, FDA will establish a DHT framework document guide the use of DHT-derived data in regulatory decision-makings for drugs and biological products. The framework will guide activities such as to:

a. Define objectives for workshops and demonstration projects;

b. Develop methodologies for evaluating DHTs proposed as measuring key (primary or important secondary) endpoints or other important measures (e.g., for safety monitoring, or baseline characterization) in clinical trials;

c. Manage submissions with extensive and continuous data, e.g., in order to develop acceptable approaches to capture adverse events; and

d. Develop a standardized process for data management and analysis of large datasets from DHTs.

2. By the end of Q2 FY 2023, FDA will establish a committee including members from CDER and CBER to support implementation of the commitments in this section. The establishment of the committee and its purpose will be made public on the FDA website. Responsibilities will include, but not be limited to:

a. Oversee the design and implementation of the DHT framework;

b. Promote consistency across centers regarding DHT-based policy, procedure, and analytic tool development;

c. Work with the FDA Digital Health Center of Excellence (DHCoE) to increase consistency across regulatory programs, to incorporate relevant learnings from review of digital tools and devices by CDRH, and to consider cross-center topics;

d. Gather information about the present state of DHTs, including specific challenges in their use; and

e. Engage with external stakeholders on DHT-related issues.

3. By the end of Q2 FY 2023, FDA will convene the first of a series of 5 public meetings or workshops with key stakeholders including patients, biopharmaceutical companies, DHT companies, and academia to gather input into issues related to the use of DHTs in regulatory decision-making. The meetings and workshops will be designed with objectives such as to:

a. Understand priorities for development of DHTs to support clinical trials, including the potential for DHTs to increase diverse patient populations in clinical trials;

b. Identify approaches to DHT validation;

c. Gain understanding of DHT data processing and analysis and inform need for novel analytical techniques; and

d. Address the regulatory acceptance of safety monitoring tools.that utilize artificial intelligence/machine learning-based algorithms for pharmacovigilance purposes, e.g., continuous data streams from DHT.

4. FDA will identify at least 3 issue-focused demonstration projects to inform methodologies for efficient DHT evaluation. These projects may include engagement with researchers from academia, biopharmaceutical industry, patient groups and other stakeholders, and will:

a. Cover key issues to inform regulatory policy development and regulatory advice. E.g.,. the projects may examine such areas as validation methods, analytic approaches to missing data, the use of multi-channel inputs to characterize an endpoint, evaluation of continuous data vs discrete measurements, use and limitations of use of DHTs in DCTs, and other related efforts.

5. By the end of Q1 FY 2023, FDA will publish draft, revised or final guidance on the use of DHTs in traditional and decentralized clinical trials, addressing the validation of measurements made by DHTs, the development of novel endpoints using DHTs, the use of DHTs as new ways to measure existing endpoints, approaches to using the patients' own DHTs such as cell phones or smart watches, usability considerations for patients, detection of safety signals during continuous data acquisition, and issues related to security and confidentiality of data.

a. Beginning in FY 2024, FDA will publish additional draft guidances in identified areas of need informed by stakeholder engagement.

i. For example, acceptable approaches to capturing and reporting adverse events in clinical trials using DHTs.

b. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

6. By the end of FY 2023, FDA will publish draft, revised or final guidance on regulatory considerations for Prescription Drug Use-Related Software that includes information about software that is disseminated by a drug applicant for use with a prescription drug or biologic product that may be described in labeling, including prescribing information. This guidance will cover software that is distributed with a drug or integrated as part of a drug- or biologic-led combination product, as well as software that is distributed by an applicant independent of an approved product.

7. FDA will expand its capacity to achieve its stated objectives in this section and to enhance consistency across the human drugs and biologics program (and as appropriate with the medical devices program) with regards to development, use, and review of DHT's and associated endpoints. Through a combination of expanded staff and contract support, FDA will:

a. Build technical expertise within the human drugs and biologics program to enhance internal knowledge, capabilities for review of IND-and NDA/BLA submissions including DHT derived endpoints, policy, standards and guidance development;

b. Train FDA staff in evaluation of DHTs;

c. Develop statistical methodology for the design, analysis, and interpretation of DHT-derived clinical trial endpoints;

d. Build review capacity and expertise to respond to DHT developers and biopharmaceutical applicants who want to use DHTs; and

e. Apply a consistent approach to review of DHTs across CDER, CBER, and CDRH as appropriate.

8. FDA will enhance its IT capabilities to support the review of DHT-generated data:

a. By end of Q2 FY 2023, FDA will enhance its internal systems to support review of DHT-related submissions including capturing key information about clinical trials utilizing DHTs to support tracking the number and rate of change of DHT-related submissions.

b. In FY 2023, FDA will establish a secure cloud technology to enhance its infrastructure and analytics environment that will enable FDA to effectively receive, aggregate, store, and process large volumes of data from trials conducted using DHTs.

c. After establishing the cloud environment, FDA will pilot a secure cloud-based mechanism to support submission and review of DHT-generated data sets.

d. FDA will work to enhance, recommend and implement standards that reduce the handling necessary to make data analyzable.

V. IMPROVING FDA PERFORMANCE MANAGEMENT

A. Studies Will Include:

1. Assessment of the internal activities related to the STAR pilot program as described in Section I.D.4.

2. Assessment of the current practices of FDA and sponsors in communicating through product quality IRs during application review as described in Section I.N.1.c.

3. Evaluation of the resource capacity planning capability as described in Section II.A.2.

4. Assessment of the hiring and retention of staff for the human drug review program in CDER and CBER as described in Section III.B.

5. Assessment of challenges or barriers in FDA's adoption of cloud-based technologies as described in Section IV.A.6.b.

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

A. 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.

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

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.

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.

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 later as the Agency gains experience with the scheme and will be communicated via guidance documents to industry

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).

9. ''Serious disease or condition,'' ''available therapy,'' ''unmet medical need,'' and ''may demonstrate substantial improvement on clinically significant endpoint(s)'' have the meanings given in FDA's Guidance for Industry: Expedited Programs for Serious Conditions, Drugs and Biologics (May 2014).

MDUFA PERFORMANCE GOALS AND PROCEDURES, FISCAL YEARS 2023 THROUGH 2027

GENERAL

The performance goals and procedures agreed to by the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) of the United States Food and Drug Administration (''FDA'' or ''the Agency'') for the medical device user fee program in the Medical Device User Fee Amendments of 2022, are summarized below.

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

I. SHARED OUTCOME GOALS

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

FDA will be reporting Total Time to Decision performance as described in Section VII. FDA and industry will participate in the independent assessment of progress toward this outcome, as described in Section VI below. As appropriate, key findings and recommendations from this assessment will be implemented by FDA.

A. PMA

PMA Shared Outcome Total Time to Decision goal: FDA will report on an annual basis the average Total Time to Decision as defined in Section VIII.G for the three most recent closed receipt cohorts. The following PMA Shared Outcome Total Time to Decision goals are subject to adjustment per Section III below:

For Original PMA and Panel Track Supplement submissions received in Fiscal Years (FY) 2023 through 2024, the average shared outcome Total Time to Decision goal for FDA and industry is 290 calendar days.

For Original PMA and Panel Track Supplement submissions received in FYs 2025 through 2027, the average shared outcome Total Time to Decision goal for FDA and industry is 285 calendar days.

B. 510(k)

510(k) Shared Outcome Total Time to Decision goal: FDA will report on an annual basis the average Total Time to Decision as defined in Section VIII.G for the most recent closed receipt cohort. The following 510(k) Shared Outcome Total Time to Decision goals are subject to adjustment per Section III below:

For 510(k) submissions received in FY 2023, the average Total Time to Decision goal for FDA and industry is 128 calendar days.

For 510(k) submissions received in FY 2024, the average Total Time to Decision goal for FDA and industry is 124 calendar days.

For 510(k) submissions received in FY 2025, the average Total Time to Decision goal for FDA and industry is 112 calendar days.

For 510(k) submissions received in FY 2026, the average Total Time to Decision goal for FDA and industry is 112 calendar days.

For 510(k) submissions received in FY 2027, the average Total Time to Decision goal for FDA and industry is 112 calendar days.

II. REVIEW PERFORMANCE GOALS—FISCAL YEARS 2023 THROUGH 2027 AS APPLIED TO MDUFA COHORTS

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

A. Pre-Submissions

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

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

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

Pre-Submission Written Feedback goal: FDA will provide written feedback that addresses the issues raised in the Pre-Submission request within 70 calendar days of receipt date or five calendar days prior to a scheduled meeting, whichever comes sooner, for:

In FY 2023, 90% of Pre-Submissions in the MDUFA Cohort if the MDUFA Cohort is fewer than 3585, or 75% of Pre-Submissions in the MDUFA Cohort if the MDUFA Cohort is 3585 or more, up to 4300 submissions.

In FY 2024, 90% of Pre-Submissions in the MDUFA Cohort if the MDUFA Cohort is fewer than 4060, or 80% of Pre-Submissions in the MDUFA Cohort if the MDUFA Cohort is 4060 or more, up to 4300 submissions.

In FY 2025–2027, 90% of Pre-Submissions in the MDUFA Cohort up to 4300 submissions.

These Pre-Submission Written Feedback goals are subject to adjustment per Section III below.

The MDUFA Cohort will only include Pre-Submissions (as defined in Section VIII.E below) for devices that are accepted for review up to a maximum number of accepted submissions subject to the goal. Pre-Submissions will be accepted in accordance with the Pre-Submission acceptance checklist described in FDA's guidance ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program.''. In addition, the following types of requests for feedback available to Breakthrough-designated products and/or products included in the Safer Technologies Program (STeP) are considered accepted for review upon receipt:

Sprint discussions;

Requests for review of a data development plan; and

Requests for review of a clinical protocol agreement.

The MDUFA Cohort will not include Pre-Submissions that are withdrawn at request of applicant or closed due to lack of applicant response.

For any Pre-Submissions in the MDUFA Cohort for which FDA does not meet the Pre-Submission Written Feedback goal, FDA will communicate with the applicant in a timely manner regarding a timeline for providing written feedback.

After the Pre-Submission MDUFA Cohort reaches the maximum number of submissions subject to the goal in a fiscal year, FDA still intends to provide timely feedback for Pre-Submissions for Breakthrough-designated products and products included in the Safer Technologies Program (STeP). After the Pre-Submission MDUFA Cohort reaches the maximum number of submissions subject to the goal, FDA intends to provide feedback for other Pre-Submissions as resources permit, but not to the detriment of meeting quantitative review timelines and statutory obligations.

Written feedback provided to the applicant will include: written responses to the applicant's questions; FDA's suggestions for additional topics for the meeting or teleconference, if applicable; or, a combination of both. If all of the applicant's questions are addressed through written responses to the applicant's satisfaction, FDA and the applicant can agree that a meeting or teleconference is no longer necessary, and the written responses will be considered the final written feedback to the Pre-Submission.

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

FDA intends that feedback the Agency provides in a Pre-Submission will not change, provided the information submitted in a future IDE or marketing application is consistent with that provided in the Pre-Submission and documented in the Pre-Submission, and that the data in the future submission, changes in the science, or changes in the standards of care do not raise any important new issues materially affecting safety or effectiveness. The minutes described above will serve as the record of the Agency's Pre-Submission feedback. Modifications to FDA's feedback will be limited to situations in which FDA concludes that the feedback does not adequately address important new issues materially relevant to a determination of safety and/or effectiveness or substantial equivalence. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs.

By March 31, 2024, the Agency will issue draft guidance to update the guidance on ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program'' to include additional information to assist applicants and review staff in identifying the circumstances in which an applicant's question is most appropriate for informal communication instead of a Pre-Submission. FDA will provide an opportunity for the public to comment on the updated guidance. No later than 18 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement this guidance once final. FDA will train staff and managers on the updated guidance.

B. Original PMAs, Product Development Protocols, Panel-Track Supplements, and Premarket Reports

The performance goals in this section apply to all Original PMAs, Product Development Protocols (PDPs), Panel-Track Supplements, and Premarket Reports.

FDA will communicate with the applicant regarding whether the application has been accepted for filing review within 15 calendar days of receipt of the application. This communication consists of a written communication that a) identifies the reviewer assigned to the submission, and b) acknowledges acceptance/rejection of the submission based upon the review of the submission

against objective acceptance criteria outlined in a published guidance document and consistent with the statute and its implementing regulations.

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

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

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

If the application is filed, FDA will communicate with the applicant through a Substantive Interaction within 90 calendar days of the filing date of the application for 95% of submissions.

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

PMA decision goal: For Original PMAs, PDPs, Panel-Track Supplements, and Premarket Reports that do not require Advisory Committee input, FDA will issue a MDUFA decision within 180 FDA Days for 90% of submissions. This PMA decision goal is relevant for purposes of Section III below.

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

If in any one fiscal year, the number of submissions that require Advisory Committee input is less than 10, then it is acceptable to combine such submissions with the submissions for the following year(s) in order to form a cohort of 10 or more submissions, upon which the combined years' submissions will be subject to the performance goal. If the number of submissions that require Advisory Committee input is less than 10 for FY 2027, it is acceptable to combine such submissions in the prior year(s) to form a cohort of 10 or more submissions: in such cases, FDA will be held to the FY 2027 performance goal for the combined years' submissions.

To facilitate an efficient review prior to the Substantive Interaction, and to incentivize submission of a complete application, submission of an unsolicited major amendment prior to the Substantive Interaction extends the FDA Day review clock by the number of FDA Days that have elapsed. Submission of an unsolicited major amendment after the Substantive Interaction extends the FDA Day goal by the number of FDA Days equal to 75% of the difference between the filing date and the date of receipt of the amendment. Requests from FDA that a submission be made will not be considered unsolicited.

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

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

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

C. 180–Day PMA Supplements

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

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

D. Real-Time PMA Supplements

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

E. De Novo Requests

De Novo decision goal: FDA will issue a MDUFA decision within 150 FDA Days for 70% of De Novo requests. This De Novo decision goal is subject to adjustment per Section III below.

Deficiencies identified will be based upon a complete review of the submission and will include all deficiencies. Deficiency letters will include a statement of the basis for the deficiencies, as provided in Section V.B below. Deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a classification determination. Any subsequent deficiencies will be limited to issues raised by the information provided by the applicant in its response, unless FDA concludes that the initial deficiencies identified do not adequately address important new issues materially relevant to a classification determination. Such a determination will be supported by the appropriate management concurrence consistent with applicable guidance and SOPs. Issues related to revisions to draft labeling will typically be addressed through interactive review once major deficiencies have been adequately addressed.

At the applicant's request and as resources permit, but not to the detriment of meeting the quantitative review timelines, if a final decision has not been rendered within 180 FDA days, FDA will discuss with the applicant all outstanding issues with the submission preventing FDA from reaching a decision. This discussion will reflect appropriate management input and approval and will include action items for FDA and/or the applicant, as appropriate, with an estimated date of completion for each party to complete their respective tasks.

F. 510(k) Submissions

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

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

For 510(k) submissions received under the eSTAR program, a submission that passes the initial technical screening will be considered accepted for review as of the date the submission was received.

FDA will communicate with the applicant through a Substantive Interaction within 60 calendar days of receipt of the submission for 95% of submissions.

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

510(k) decision goal: FDA will issue a MDUFA decision for 95% of 510(k) submissions within 90 FDA Days. This 510(k) decision goal is relevant for purposes of Section III below.

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

In addition, information about submissions that miss the 510(k) decision goal will be provided as part of FDA's Performance Reports, as described in Section VII.

G. CLIA Waiver by Application

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

Pre-Submission review timeframes in Section II.A apply to Pre-Submissions for CLIA Waiver by Application and Dual submission 510(k)/CLIA Waiver applications.

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

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

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

If in any one fiscal year, the number of submissions in any CLIA Waiver by Application category is less than 10, then it is acceptable to combine such submissions with the submissions for the following year(s) in order to form a cohort of 10 or more submissions, upon which the combined years' submissions will be subject to the performance goal.

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

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

H. Original Biologics Licensing Applications (BLAs)

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

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

I. BLA Efficacy Supplements

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

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

J. Original BLA and BLA Efficacy Supplement Resubmissions

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

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

K. BLA Manufacturing Supplements Requiring Prior Approval

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

III. OPPORTUNITY FOR PERFORMANCE IMPROVEMENTS

MDUFA V will provide for increases in fee revenue above the annual total revenue amount to support performance improvements in FY 2025, FY 2026, and/or FY 2027, as detailed below. If such fee revenue adjustments are not made, the performance goals in Section II apply.

For the purpose of fee revenue adjustments, performance of all goals in this section, except for the Pre-Submission Written Feedback goal, will be determined based on data available as of 18 months following the close of the fiscal year at issue. Thus, for a FY 2023 goal, the performance will be determined based on data available as of March 31, 2025. For a FY 2024 goal, the performance will be determined based on data available as of March 31, 2026. For the Pre-Submission Written Feedback goal, performance will be determined based on data available as of 6 months following the close of the fiscal year at issue. Thus, for example, for the Pre-Submission Written Feedback goal for FY 2023, performance will be determined based on data available as of March 31, 2024.

A. PMA and 510(k): Decision Goals and Shared Outcome Total Time to Decision Goals

I. FDA's 510(k) decision goal, the FDA/Industry 510(k) Shared Outcome Total Time to Decision goal, FDA's PMA decision goal, and the FDA/Industry PMA Shared Outcome Total Time to Decision goal are met for FY 2023, and fee revenue above the annual total revenue amount is provided in FY 2026 and FY 2027 to support performance improvements, the 510(k) Shared Outcome Total Time to Decision goal will be adjusted to 108 days for FY 2026 and FY 2027 and the PMA Shared Outcome Total Time to Decision goal will be adjusted to 275 days for FY 2026 and FY 2027.

If FDA's 510(k) decision goal, the FDA/Industry 510(k) Shared Outcome Total Time to Decision goal, FDA's PMA decision goal, and the FDA/Industry PMA Shared Outcome Total Time to Decision goal are met in FY 2024, and fee revenues above the annual total revenue amount are provided in FY 2027 to support performance improvements, the 510(k) Shared Outcome Total Time to Decision goal will be adjusted to 108 days and the PMA Shared Outcome Total Time to Decision goal will be adjusted to 270 days for FY 2027.

B. De Novo Requests

If the De Novo decision goal is met for FY 2023, and fee revenue above the annual total revenue amount is provided in FY 2026 and FY 2027 to support performance improvements, the goal will be adjusted to 80% of De Novo requests receiving a MDUFA decision within 150 FDA days for FY 2026 and 2027.

If the De Novo decision goal is met for FY 2024, and fee revenue above the annual total revenue amount is provided in FY 2027 to support performance improvements, the goal will be adjusted to 90% of De Novo requests receiving a MDUFA decision within 150 FDA days in FY 2027.

C. Pre-Submissions

If the Pre-Submission Written Feedback goal is met for FY 2023, and fee revenue above the annual total revenue amount is provided to support performance improvements, the maximum number of submissions subject to the goal will escalate to 4700 Pre-Submissions in FYs 2025, 2026 and 2027.

If the Pre-Submission Written Feedback goal is met for FY 2024, and fee revenue above the annual total revenue amount is provided to support performance improvements, the maximum number of submissions subject to the goal will escalate to 4800 Pre-Submissions in FY 2026 and FY 2027.

If the Pre-Submission Written Feedback goal is met for FY 2025, and fee revenue above the annual total revenue amount is provided to support performance improvements, the goal will not be subject to a maximum number of submissions in FY 2027.

The goal for percent of Pre-Submissions in the MDUFA Cohort receiving timely feedback, as described in Section II.A, will remain at 90% for FYs 2025, 2026, and 2027.

IV. INFRASTRUCTURE

A. Quality Management

The CDRH Quality Management and Organizational Excellence (QMOE) Program is comprised of a team of certified quality management staff who report to the Center Director. This QMOE staff are focused on meeting customers' needs by improving consistency, efficiency, timeliness, and effectiveness of operations. The QMOE Program establishes and leads the CDRH Quality Management System (QMS) activities, facilitates process improvements, independently audits CDRH processes and activities, and assesses the effectiveness of actions taken to prevent potential (risk management) and resolve existing issues (nonconformity management).

At least once per year, the Agency will discuss with industry the specific areas it intends to incorporate in its ongoing audit plan with the QMOE Program. FDA will identify, with industry input, areas to audit, which will include the effectiveness of CDRH's nonconformity management process. FDA will continue to expand the scope of its annual audits as it implements and builds up its auditing capability, as resources permit. At a minimum, FDA audits in the following areas will be completed: Pre-Submissions and Third Party Review Program.

As part of these ongoing audits, high-performing premarket review best practices utilized in one Office of Health Technology (OHT) will be identified and shared accordingly with other OHTs to improve efficiencies and effectiveness.

At least once per year, FDA will report on the results of the audits, best practices identified and shared across OHTs, and the actions taken in response to nonconformities associated with the nonconformity management process.

B. Financial Transparency and Hiring

1. Financial Transparency

FDA will publish a MDUFA 5-year financial plan no later than the end of the 2nd quarter of FY 2023. The financial plan will include the Agency's annual hiring targets. No later than the end of the 2nd quarter of each subsequent fiscal year, FDA will publish updates to the 5-year plan as of the end of the prior fiscal year. The annual updates will include information concerning:

The number of new MDUFA V hires by Office;

The number of new MDUFA V hires made from outside the Center, as well as the number of new MDUFA V hires made from current Center employees (if any);

The number of unfilled new MDUFA V hires;

The changes in the personnel compensation and benefit costs for the process for the review of medical device applications that exceed the amounts provided by the personnel compensation and benefit costs portion of the inflation adjustment;

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

An accounting of the amount excluded from the designated amount within the operating reserves, which is intended to support the Third Party Review program and the Total Product Life Cycle Advisory Program Pilot.

2. Carryover Balance

MDUFA V will provide for FDA to decrease registration fees if the Agency has more than 13 weeks of operating reserves in the carryover balance. In addition, during MDUFA V FDA will use funds in the carryover balance to support the Third Party Review program and the Total Product Life Cycle Advisory Program Pilot. The amount of carryover balance funds intended to support these programs will be excluded when

calculating the amount of operating reserves to determine if registration fees will be decreased. The current statutory one-month reserve will also be excluded when calculating the amount of operating reserves to determine if registration fees will be decreased. User fee funds in the carryover balance that are considered unappropriated or unearned are not included in the operating reserves.

No less than annually, FDA and industry will work together to seek alignment on how best to utilize available funds in the carryover balance to improve the process for the review of device applications—e.g., performance on submission types with performance goals and/or quality management programs. FDA and industry will use, as input for the discussion, workload information, performance objectives, and ongoing reported performance.

3. Hiring Goals

Enhancements to the medical device review program require that FDA recruit, hire and retain sufficient numbers and types of technical, scientific, and other program experts to support the process for the review of device applications. MDUFA V provides significant new resources to FDA to support these activities.

To help ensure that FDA accomplishes hiring in accordance with the assumptions underlying the agreement, FDA will establish annual hiring goals for each year of MDUFA V.

The minimum hiring goals for FY 2023–2025 are:

FY 2023: 144 hires

FY 2024: 42 hires

FY 2025: 24 hires

As described in Section III, the MDUFA V agreement provides for enhancements to the shared outcome total time to decision goals and to specified review performance goals, provided that specified goals were met in prior years. These enhanced goals will be applicable in FY 2025 (for the Pre-Submission Written Feedback goal) and FY 2026–2027 (for the Pre-Submission Written Feedback goal, the PMA Shared Outcome Total Time to Decision goal, the 510(k) Shared Outcome Total Time to Decision goal, and the De Novo Decision goal).

FDA and Industry have agreed that, if performance improvement adjustments are triggered for each year per Section III, the Agency will increase hiring to support the enhanced goals.

FY 2025

In FY 2025, if performance improvement adjustments are made to the Pre-Submission Written Feedback goal per Section III, FDA will increase the hiring goal by 59 hires to a total of 83 hires. As part of the process for establishing the user fee rates for FY 2025, FDA will also calculate the hiring goal for that year and include the goal in the associated Federal Register fee-setting notice.

FY 2026 and FY 2027

In FY 2026 and FY 2027, the number of hires will depend on (1) which performance improvement adjustments are triggered for that year, and (2) whether the hiring goal was increased the prior year. For FY 2026 and FY 2027, as part of the process for establishing the user fee rates for that year, FDA will also calculate the hiring goal for that year and include the goal in the associated Federal Register fee-setting notice.

Pre-hires

For purposes of determining whether the hiring goal is met for FY 2023, FDA will include ''pre-hires'' that are made in FY 2022 for MDUFA V positions. In addition, for subsequent fiscal years, if FDA exceeds the hiring goal, the additional hires made above the goal will be counted towards the following fiscal year goal.

4. Fee Adjustment Related to Hiring

For FY 2023, if the hiring goal is missed by more than 15% at the end of the fiscal year (i.e., if fewer than 123 hires are made in FY 2023, including FY 2022 pre-hires), unused fees that were projected to support these hires for FY 2023 will be used to decrease registration fees for FY 2025.

For FY 2024 or FY 2025, if the hiring goal is missed by more than 10% at the end of the fiscal year (i.e., if fewer than 38 hires are made in FY 2024), unused fees that were projected to support these positions for the applicable fiscal year will be used to decrease registration fees for FY 2026 and FY 2027, respectively.

The amount of the hiring adjustment fee decrease will be the product of the number of hires by which the hiring goal was missed and one-quarter of the inflation-adjusted cost per full-time equivalent (FTE).

For the purpose of calculating progress toward meeting these hiring goals, a hire is defined as someone who has been confirmed as on board by the date indicated in a full-time position. Hires may be recruited from outside the FDA, or, in some cases, a hire can also be a current FDA employee who is changing positions within the agency.

C. IT Infrastructure for Submission Management

FDA will continue to enhance IT infrastructure to support the process for the review of device applications.

FDA will maintain and improve on the Customer Collaboration Portal, including the submission progress tracking system that provides near real-time submission status. By the end of MDUFA V, the progress tracking system will include 510(k), Original PMA and Panel-Track Supplements, De Novo, Pre-Submissions, and IDEs.

FDA will continue to develop electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review process. Templates for Original PMA and Panel-Track Supplements, De Novo, Pre-Submissions, and IDEs will be completed and made available for voluntary use by the end of MDUFA V.

D. Training

FDA will continue to evaluate and improve training for new and existing reviewers under this agreement. FDA training efforts will also be closely coordinated with the QMOE Program to provide more targeted and personalized training to staff.

E. Time Reporting

FDA will continue to perform complete time reporting such that data from time reporting can be used to conduct workload analysis and capacity planning.

V. PROCESS IMPROVEMENTS

A. Interactive Review

The Agency will continue to incorporate an interactive review process to provide for, and encourage, informal communication between FDA and applicants to facilitate timely completion of the review process based on accurate and complete information. Interactive review entails responsibilities for both FDA and applicants. As described in the 2014 guidance document, ''Types of Communication During the Review of Medical Devices Submissions,'' both FDA and industry believe that an interactive review process for premarket medical device submissions should help facilitate timely completion of the review based on accurate and complete information. Interactive review is intended to facilitate the efficient and timely review and evaluation by FDA of premarket submissions and is expected to support reductions in total time to decision. The interactive review process contemplates increased informal interaction between FDA and applicants, including the exchange of scientific and regulatory information.

B. Deficiency Letters

By January 1, 2023, the Agency will update the 2017 guidance ''Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions; Guidance for Industry and FDA Staff'' to clarify what constitutes a statement of the basis for the deficiency and continue alignment with the following:

Deficiency letters should include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position.

Deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a marketing authorization decision (e.g., 510(k) clearance, PMA approval, and de novo classification).

FDA will train staff and managers on the updated guidance and work to make improvements (including incorporating best practices), as appropriate, to address findings from audits and consistent with the guidance.

FDA will provide a statement of the basis for the deficiency, consistent with the updated guidance, in deficiency letters as follows: 75% of deficiencies in FY 2023, 80% of deficiencies in FY 2024, 85% of deficiencies in FY 2025, 90% of deficiencies in FY 2026, and 95% of deficiencies in FY 2027 for Original PMA, Panel-Track Supplement, 510(k) and De Novo request submissions. Performance will be determined by means of annual audit conducted by QMOE. Sampling procedures will incorporate ISO 2859-1:1999 (''Sampling Procedures for inspection by attributes—Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection''). FDA will review each fiscal year's audit results with industry no later than the first quarterly meeting of the following fiscal year.

C. Enhanced Use of Consensus Standards

The voluntary Accreditation Scheme for Conformity Assessment (ASCA) Pilot is intended to enhance product reviewers' and device manufacturers' confidence in medical device testing when manufacturers rely on testing completed by ASCA-accredited testing laboratories. This should generally decrease the need for the FDA to request additional information regarding testing methodologies when a premarket submission includes ASCA testing. ASCA also incorporates existing international conformity assessment standards and practices where practical.

FDA will use lessons learned from implementation of the ASCA Pilot Program during MDUFA IV to transition from a pilot to a sustainable and expanded program. Specifically, the Agency will:

1. By the end of FY 2023, FDA will complete the pilot. In Q2 of FY 2024, FDA will provide a report on the performance of the ASCA Pilot Program (to replace the report specified in the MDUFA IV Commitment Letter, Commitment IV.D.8.a). In the report, FDA will provide at least the following information:

a. Adequacy of the standards selected to support confidence by FDA and industry in the methods used and results reported by ASCA-accredited testing laboratories;

b. Testing laboratory participation in the training and ASCA program, and areas where any nonconformities were observed;

c. Number of submissions containing the ASCA Summary Report;

d. Summary Report acceptance rate by FDA reviewers; and

e. Summary of commonly cited deficiencies regarding the Summary Report.

2. FDA will train staff and supervisors so that specific deficiencies are relevant to the requirements of the Summary Report.

3. FDA will continue to provide adequate training to testing laboratories and reviewers to accurately execute the ASCA process.

4. FDA will report annually on the progress of the ASCA program.

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

D. Third Party Review

The Agency will continue to support the Third Party Review program, with the objective of eliminating routine re-review by FDA of Third Party reviews through continuation of the following activities:

1. Provide training for Third Parties seeking accreditation by FDA. This training shall include the opportunity for Third Parties to have access to redacted review memos and other information as appropriate.

2. When FDA's expectations for a particular device type change, FDA will maintain a process to convey this information to the Third Parties and to industry.

3. Audit and provide tailored re-training to accredited Third Parties based on the results of audits.

4. Publish performance of individual accredited Third Parties with at least five completed submissions on FDA's website (e.g., rate of NSE, average number of holds, average time to SE).

FDA will consider the factors described in the guidance, ''510(k) Third Party Review Program,'' in determining device type eligibility for the Third Party Review program. Consistent with that guidance, some device types that rely on clinical data to demonstrate substantial equivalence may be eligible for Third Party Review.

E. Patient Science and Engagement

The Agency will take the following actions to continue engaging patients and incorporating their perspectives in the regulatory process. Where appropriate, the Agency will leverage collaborations and partnerships with patients, healthcare providers, industry, and others, as well as collaborations across FDA Centers, to advance these actions.

1. Expand clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing applicant-proposed use of voluntary patient preference information (PPI), voluntary patient reported outcomes (PROs), and/or patient generated health data (PGHD). These staff will provide submission review and early consultation/advice to industry during study planning.

2. Issue a draft guidance providing best practices on incorporating into premarket studies clinical outcome assessments including their use as primary or co-primary endpoints. A clinical outcome assessment (COA) describes or reflects how a person feels, functions, or survives and can be reported by a health care provider or a non-clinical observer (such as a parent), through performance of an activity or task, or by the patient.

3. Support the use of innovative technologies to capture patient input and reduce patient burden to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention.

4. By the end of FY 2024, hold a public meeting to explore ways to use patient-generated health data to help advance remote clinical trial data collection and support clinical outcome assessments.

5. FDA will undertake the following activities to improve the regulatory predictability and impact of patient science:

a. Develop case examples of modified or adapted PRO instruments to make efficient use of existing validated PRO instruments which may be improved or adapted to other subpopulations or other regulatory uses in a more streamlined and expeditious manner than creating novel PROs.

b. Strengthen efforts to expand staff understanding of Patient Science and Engagement (PSE) topics, and consistent evaluation in submissions through training curriculum and internal infrastructure to improve consistency (e.g., Focal Point Program).

c. Update FDA's existing guidance, ''Patient Preference Information—Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling,'' with pragmatic insights and to address common questions for those interested in the voluntary use of PPI in regulatory submissions.

d. Explore opportunities to improve patient science tools for medical devices and advance health equity through targeted incorporation of diverse patient perspectives and integration of data from diverse patients.

e. Identify high impact opportunities to incorporate patient perspectives.

6. Facilitate industry efforts to collaborate with patients in key areas by generating patient-friendly educational modules on device trials, real-world data, device development tools, and regulatory frameworks. FDA will also make these educational modules publicly available, as appropriate.

7. The existing dispute resolution process should be used in the event of disagreement between the applicant and the Agency on the need for PPI, PRO and/or other tools to capture PGHD.

F. Real World Evidence (RWE)

The Agency will use user fee revenue for the continued development of Real-World Data (RWD) and RWE methods and policies to advance regulatory acceptance for premarket submissions, including expanded indications for use and new clearance/approval of new devices, and clarify related reporting requirements.

1. FDA will update the 2017 guidance document Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices to provide more clarity on:

a. Least burdensome general expectations on what is needed to demonstrate the ''Fit-for-Purpose of RWD'' for premarket regulatory purposes, including expanded indications for use and new clearance/approval of new devices;

b. More information, including generalized examples, on previously used and accepted methodologies; and

c. Best practices for RWE review.

2. FDA will continue to advance CDRH's RWD/RWE Training program for FDA review teams including the medical review staff. Topics will include best practices for RWE review and when to engage with CDRH RWE subject matter experts.

3. FDA will provide transparent program development updates and financial accounting of User Fee revenue specifically intended for the activities in this section.

a. FDA will update stakeholders on the RWE program activities at two or more open public meetings during the course of MDUFA V.

b. FDA hiring of internal experts to support the review of RWD/RWE-related submissions will be tracked.

c. In any portion of the user fee funding is distributed to the National Evaluation System for health Technology (NEST), the funding should be used to transparently:

i. Support the development of RWD resources to facilitate appropriate access for research studies;

ii. Convene experts to develop best practices and, advance innovative methodology approaches with respect to RWE development and analysis;

iii. Include, on the organization's governing board, no fewer than 4 representatives of the trade associations that participated in the MDUFA V negotiations (AdvaMed, MDMA, MITA, and ACLA), with each association appointing an individual to serve. Industry representation on the governing board, if applicable, will make up at least 25% of the governing board membership at all times, and shall be selected by the industry associations. The representative from each trade association may be part of the staff of the association or appointed from a member company. If any of the trade associations elects not to participate on the governing board or for any additional seats allocated to industry, the participating trade associations will determine how to fill any vacant Industry positions.

d. By the end of FY 2023, FDA will publish a document requesting public comment on how FDA should use any portion of the user fee funding that may be distributed to any external organization(s) other than NEST to support premarket RWE.

e. If any portion of the user fee funding is distributed to an external organization(s) other than NEST, the funding will be accounted for in FDA's quarterly MDUFA report.

G. Digital Health

The Agency will continue to build its digital health expertise and continue working to streamline and align FDA review processes with software lifecycles for digital health products. Specifically, the Agency will:

1. Continue to develop software and digital health technical expertise to provide assistance for premarket submissions that include software, interoperable devices, or otherwise incorporate digital health technologies, such as artificial intelligence or machine learning (AI/ML), Virtual, Mixed, and Augmented Reality (VR/MR/AR) and wearables.

2. Strengthen efforts to expand staff understanding of digital health topics and enhance consistent evaluation in submissions through training and internal infrastructure (e.g., Focal Point Program).

3. Continue to participate in international harmonization efforts related to digital health, including work on developing software and other digital health convergence efforts.

4. Finalize the draft guidance, ''Content of Premarket Submissions for Device Software Functions,'' by 18 months from close of the comment period.

5. Publish draft guidance describing a process to evaluate a predetermined change control plan for digital health devices.

6. Engage with stakeholders, including patients, users, and industry, through roundtables, informal meetings, and teleconferences to explore regulatory approaches to digital health technologies.

H. Guidance Document Development

FDA will apply user fee revenues to ensure timely completion of Draft Guidance documents. The Agency will strive to finalize, withdraw, reopen the comment period, or issue a new draft guidance for 80% of draft guidance documents within 3 years of the close of the comment periods as resources permit. The Agency will strive to finalize,

withdraw, reopen the comment period, or issue a new draft guidance for 100% of draft guidance documents within 5 years of the close of the comment periods as resources permit. The Agency will continue to develop guidance documents and improve the development process as resources permit, but not to the detriment of meeting quantitative review timelines and statutory obligations.

I. International Harmonization

FDA is committed to improving the efficiency of the global regulatory systems for medical devices through international harmonization and convergence of regulatory requirements. The Agency will take the following actions to advance such international harmonization. Specifically, the Agency will:

1. Expand engagement in international harmonization and convergence efforts through participation with international regulators and other key stakeholders in forums, working groups, projects, and committees to promote alignment with international best practices and internationally developed policies, including exploring the development of harmonized premarket review processes.

2. Further support regulatory convergence by creating a mechanism for FDA to work with regulatory partners with whom we have appropriate confidentiality commitments to inform and align international regulatory strategy. This may include, for example, sharing of scientific, clinical, or other technical information, or policies and practices, as needed and consistent with applicable disclosure law and policy.

3. Commencing in FY 2023, assess the extent of CDRH implementation of International Medical Device Regulators Forum (IMDRF) technical documents and make this information publicly available to enhance clarity and transparency.

4. Support the creation of a forum to engage with relevant stakeholders, including industry representatives and other regulators, to identify opportunities for regulators to leverage one another's approach to decision making.

5. Participate in outreach activities to other regulatory authorities that encourage harmonization and may also encourage such authorities to rely in whole or in part on FDA marketing authorizations.

6. By the end of FY 2023, issue for public comment a draft strategic plan with additional details and timelines associated with achieving the international harmonization objectives described above.

7. Commencing with FY 2024, publish an annual assessment of the international harmonization activities described the strategic plan above, including the progress assessment described in subparagraph 3 above.

J. Total Product Life Cycle (TPLC) Advisory Program

FDA will establish a pilot of the Total Product Life Cycle (TPLC) Advisory Program (TAP Pilot) during the course of MDUFA V.

1. Vision: The long-term vision for a successful TPLC Advisory Program (TAP) is to help spur more rapid development as well as more rapid and widespread patient access to safe, effective, high-quality medical devices of public health importance. A mature TAP will also help ensure the sustained success of the Breakthrough devices program.

2. TAP Pilot Objective: The TAP Pilot is intended to demonstrate the feasibility and benefits of process improvements to FDA's early interactions with participants and FDA's facilitation of interactions between participants and stakeholders that support the vision for TAP. Through the TAP Pilot, the FDA will provide the following types of strategic engagement for innovative devices of public health importance:

Improving participants' experiences with FDA by providing for more timely premarket interactions;

Enhancing the experience of all participants throughout the device development and review process, including FDA staff;

Facilitating improved strategic decision-making during product development, including earlier identification, assessment, and mitigation of product development risk;

Facilitating regular, solutions-focused engagement between FDA review teams, participants, and other stakeholders such as patients, providers, and payers, beginning early in device development; and

Collaborating to better align expectations regarding evidence generation, improve submission quality, and improve the efficiency of the premarket review process

3. Goals: To achieve the above TAP Pilot objective, FDA will:

a. Begin and support a TAP Pilot, scoped to include the following:

In FY 2023, enroll up to 15 products in a ''soft launch'' in one Office of Health Technology (OHT); selection of the OHT will include consideration of the OHT's historical number of granted Breakthrough designations, workload, and available staffing and expertise;

In FY 2024, continue to support products enrolled in the previous fiscal year and expand to enroll up to 45 additional products in at least two OHTs (i.e., up to 60 total products enrolled through FY 2024);

In FY 2025, continue to support products enrolled in previous fiscal years and expand to enroll up to 65 additional products in at least four OHTs (i.e., up to 125 total products enrolled through FY 2025); and

In FY 2026–FY 2027, continue to support products enrolled in previous fiscal years and expand to enroll up to 100 additional products each fiscal year within existing OHTs or expand to additional OHTs, depending on lessons learned from FY 2023–FY 2025 experience (i.e., up to 225 total products enrolled through FY 2026 and up to 325 total products enrolled through FY 2027).

For FY 2024–FY 2027, in addition to the considerations above, selection of the OHTs will include consideration of experience from prior years and input from industry and other stakeholders.

b. Beginning in FY 2024, implement and track the following quantitative performance metrics:

FDA will engage in a teleconference with the participant on requested topic(s) pertaining to the TAP device within 14 days of the request for 90% of requests for interaction.

FDA will provide written feedback on requested biocompatibility and sterility topics(s) pertaining to the TAP device within 21 days of the request for 90% of such requests for written feedback.

FDA will provide written feedback on requested topic(s) pertaining to the TAP device other than biocompatibility and sterility within 40 days of the request for 90% of requests for written feedback.

c. Regularly review TAP pilot progress with industry, share feedback, and assess the impact of the TAP Pilot and opportunities for improvement.

d. Publish an assessment of the TAP Pilot on the FDA web site no later than January 30, 2026.

For purposes of the annual performance report and corrective action report, the goals of the TAP pilot are set forth in Section V.J.3 above.

4. Enrollment. FDA intends to enroll participants in the pilot using the following criteria:

a. Participation in the pilot will be voluntary.

b. For FY 2023–FY 2025, products will be those with a granted Breakthrough designation. For FY 2026–FY 2027, products will be those with a granted Breakthrough designation or request for inclusion in the Safer Technologies Program (STeP).

c. Participants have not submitted a Pre-Submission about the product after granted Breakthrough designation or request for inclusion in STeP.

d. Products will be early in their product development process (e.g., have not yet initiated a pivotal study) at time of pilot enrollment.

e. Each participant will have a maximum of one product enrolled in the pilot per fiscal year.

f. Participants will be enrolled on first-come, first-served basis.

FDA will inform potential participants of the TAP Pilot as part of the Breakthrough designation process or request for inclusion in STeP process.

If spaces remain available in a participating OHT or if resources permit, FDA may consider enrolling devices from additional OHT(s).

5. TAP Pilot Assessment. For informational purposes, FDA will conduct an assessment of the TAP Pilot using an independent third party (or parties) to assess the TAP pilot. This assessment will include a participant survey and quantitative and qualitative success metrics, starting in FY 2024, that include but are not limited to:

a. The extent to which FDA is successful at meeting the quantitative goals described in V.J.3.b. above.

b. Participant satisfaction with the timeliness, frequency, quality, and efficiency of interactions with and written feedback from FDA.

c. Participant satisfaction with the timeliness, frequency, quality, and efficiency of voluntary interactions with non-FDA stakeholders facilitated by FDA (if utilized).

d. An overall assessment of the outcomes of the Pilot and opportunities for improvement.

6. Other Measures. For informational purposes, FDA will begin to track other measures of program success, which will include:

Time from granting of Breakthrough designation or request for inclusion in the Safer Technologies Program (STeP) to receipt of marketing submission;

Time from receipt of marketing submission to marketing authorization; and

Requests for additional information during submission review.

VI. INDEPENDENT ASSESSMENTS

A. Independent Assessment of MDUFA Workforce Metrics

FDA will retain a qualified, independent contractor with expertise in assessing public sector workforce data analysis and reporting to conduct an assessment of current methodologies and data/metrics available to represent the MDUFA workforce. This will include assessment of positions (filled/vacant) and MDUFA process FTEs, including the subset funded by user fees, for each applicable FDA Center and Office.

The report will include the contractor's findings from the assessment and recommendations for improved methodologies to represent MDUFA FTE resources, including the subset funded by user fees. The assessment will be published on FDA's website by March 31, 2025.

B. Independent Assessment of Review Process Management

FDA and the industry will participate in a targeted assessment of the process for the review of device applications. The assessment

will include consultation with both FDA and industry at the start of the assessment and prior to issuance of the final report. The assessment shall be conducted under contract to FDA by a private, independent consulting firm capable of performing the technical analysis, management assessment, and program evaluation tasks required to address the assessment scope described below within the budget provided under this user fee agreement.

The contractor will:

1. Evaluate FDA's premarket review program to identify efficiencies that were realized as a result of the process improvements and investments under MDUFA IV and V;

2. Assess the alignment of resource needs with the training and expertise of hires;

3. Identify and share best practices across OHTs in OPEQ;

4. Assess the effectiveness of program areas targeted for improvement under this agreement, including the following:

a. Implementation and impact of changes to the guidance ''Developing and Responding to the Deficiencies in Accordance with the Least Burdensome Provisions,''

b. Implementation and impact of changes to the guidance ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program,''

c. Third Party Review program (continued reduction of routine re-review by FDA of Third Party reviews),

d. Digital Health program,

e. Patient Science and Engagement program,

f. Real World Evidence program, and

g. International Harmonization.

5. Assess other key areas identified by FDA and industry as resources permit.

FDA will award the contract no later than March 31, 2025. However, the contractor would not begin the audit of Pre-Submissions before October 1, 2025. The contractor will publish comprehensive findings and recommendations within 1 year, after reviews with FDA and industry and opportunities to provide feedback for the contractor's consideration prior to finalizing the final report. For all recommendations the contractor will provide an estimate of additional resources needed or efficiencies gained, as applicable.

FDA will incorporate findings and recommendations, as appropriate, into its management of the process for the review of device applications. FDA will analyze the recommendations for improvement opportunities identified in the assessment and, as appropriate, develop and implement a corrective action plan, and assure its effectiveness.

VII. PERFORMANCE REPORTS

The Agency will report its progress toward meeting the goals described in this letter, as follows. If, throughout the course of MDUFA V, the Agency and Industry agree that a different format or different metrics would be more useful, the reporting will be modified accordingly as per the agreement of both FDA and Industry.

1. Quarterly reporting at the CDRH OHT level/CBER Center level (in recognition of the significantly smaller number of submissions reviewed at CBER):

1.1. For 510(k) submissions that do not go through a Third Party, reporting will include:

i. Average and quintiles of the number of calendar days to Substantive Interaction

ii. Average, and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision

iii. Average number of review cycles

iv. Rate of submissions not accepted for review

1.2. For PMA submissions, reporting will include:

i. Average and quintiles of the number of calendar days to Substantive Interaction for Original PMA, Panel-Track PMA Supplement, and Premarket Report Submissions

ii. Average and quintiles of the of FDA Days, Industry Days, and Total Days to a MDUFA decision

iii. Rate of applications not accepted for filing review, and rate of applications not filed

1.3. For De Novo requests, reporting will include:

i. Average, and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision

ii. Average number of review cycles

iii. Rate of submissions not accepted for review

1.4. For Pre-Submissions, reporting will include:

i. Number of Pre-Submissions in the MDUFA cohort

ii. Rate of submissions not accepted for review

iii. Average and quintiles of the number of calendar days from submission to written feedback

iv. Number of Pre-Submissions that require a meeting

v. Percent of submissions with meetings for which industry provided minutes within 15 days

1.5. For IDE applications, reporting will include:

i. Number of original IDEs received

ii. Average number of amendments prior to approval or conditional approval of the IDE

1.6. In FY 2023, for marketing submissions for In Vitro Diagnostics, FDA will report on the status of submissions received in FY 2020–2021 that remain under review as a result of being paused while the Agency focused on COVID–19–related submissions.

2. CDRH will report quarterly, and CBER will report annually, the following data at the Center level:

2.1. Rate of NSE decisions for 510(k) submissions

2.2. Rate of withdrawals for 510(k), De Novo, and PMA submissions

2.3. Rate of Not Approvable decisions for PMA submissions

2.4. Rate of Denial decisions for De Novo requests

2.5. Key product areas or other issues that FDA identifies as noteworthy because of a potential effect on performance, including significant rates of Additional Information requests

2.6. Specific topic or product area as it relates to performance goals, agreed upon at the previous meeting

2.7. Number of submissions that missed the goals and the total number of elapsed calendar days broken down into FDA days and industry days

2.8. Newly released draft and final guidance documents, and status of other priority guidance documents

2.9. Agency level summary of fee collections

2.10. Independent assessment implementation plan status

2.11. Results of independent assessment and subsequent periodic audits and progress toward implementation of the recommendations and any corrective action

2.12. Number of fee waivers or reductions granted by type of submission

3. The Agency will report quarterly the following data for the MDUFA program:

3.1. Progress towards meeting annual hiring goals

3.2. Per Section V.F.3.e, if any portion of the user fee funding intended for real world evidence activities is distributed to an external organization(s) other than NEST, information regarding use of the user fee funding

4. In addition, the Agency will provide the following information on an annual basis:

4.1. Review time devoted to direct review of applications

4.2. The number of Premarket Report Submissions received

4.3. Summary information on training courses available to CDRH and CBER employees, including new reviewers, regarding device review and the percentage of applicable staff that have successfully completed each such course. CDRH will provide information concerning any revisions to the new reviewer training program curriculum.

4.4. Performance on the shared outcome goal for average Total Time to Decision

4.5. For 510(k) submissions, reporting will include:

i. Number of submissions reviewed by a Third Party

ii. Number of Special Submissions

iii. Number of Traditional Submissions

iv. Average and number of days to Accept/Refuse to Accept

v. Number of Abbreviated Submissions

4.6. For 510(k) submissions that go through a Third Party, reporting will include:

i. Time from FDA receipt of Third Party report to FDA decision at the 90% percentile

ii. Rate of NSE

iii. Average number of holds

iv. Average time to SE

4.7. For PMA submissions, reporting will include the number of the following types of PMA submissions received:

i. Original PMAs

ii. Priority PMAs

iii. Premarket Reports

iv. Panel-Track PMA Supplement

v. PMA Modules

vi. 180-Day PMA Supplements

vii. Real-Time PMA Supplements

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

4.8. For De Novo requests, reporting will include:

i. Number of submissions received

ii. Average and number of days to Accept/Refuse to Accept

4.9. For CLIA waiver applications, reporting will include:

i. Number of CLIA waiver applications received

ii. Average and quintiles of the number of calendar days to Substantive Interaction

iii. Average and quintiles of the number of FDA Days, Industry Days, and Total Days to a MDUFA decision and a discussion of any trends in the data

4.10. Report on the ASCA program

4.11. Data regarding the reviewer to manager ratio

4.12. Report on QMOE program

4.13. Summary of QMOE audits, including annual audit of Deficiency Letters under Section V.B above

4.14. Summary of primary cost drivers that contribute to change in personnel compensation and benefits costs (e.g., cost of living adjustments and increases in agency benefits contributions, if applicable)

4.15. The return on investment, which may include process improvements, improved performance, and other enhancements, under MDUFA V.

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

Number and percentage of LDT 510(k)s and non-LDT IVD 510(k)s completed within 90 FDA days

Number and percentage of LDT De Novo requests and non-LDT IVD De Novo requests completed within 150 FDA days

Number and percentage of LDT PMAs and non-LDT IVD PMAs completed within 180 FDA days

To the extent that laboratories make submissions regarding LDTs that are covered by the MDUFA V agreement, FDA will treat such LDT submissions no less favorably than other submissions to which MDUFA V performance goals apply.

VIII. DEFINITIONS AND EXPLANATIONS OF TERMS

A. Applicant

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

an application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (FD&C Act);

a premarket notification under section 510(k) of the FD&C Act;

an application for investigational device exemption under section 520(g) of the FD&C Act;

a Pre-Submission;

a De Novo classification request (De Novo request) under section 513(f)(2) of the FD&C Act;

a CLIA Waiver by application.

B. eSTAR (electronic Submission Template And Resource)

An electronic submission template built within a structured dynamic PDF that guides a user through construction of an eSubmission. eSTAR is the only type of electronic submission template that is currently available to facilitate the preparation of 510(k) submissions as eSubmissions. For simplicity, the electronic submission created with this electronic submission template is often referred to as an eSTAR.

C. FDA Days

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

D. MDUFA Decisions

Original PMAs, Product Development Protocols, Panel-Track Supplements, and Premarket Report Applications: Decisions are approval, approvable, approvable pending GMP inspection, not approvable, withdrawal, and denial.

180-Day PMA Supplements: Decisions for 180-Day PMA Supplements are approval, approvable, and not approvable.

Real-Time PMA Supplements: Decisions for Real-Time PMA supplements are approval, approvable, and not approvable.

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

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

CLIA Waiver by Application Submissions: Decisions for CLIA Waiver by Application Submissions are approval, withdrawal, and denial.

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

E. Pre-Submission

A Pre-Submission includes a formal written request from an applicant for feedback from FDA that is provided in the form of a formal written response or, if the manufacturer chooses, formal written feedback followed by a meeting or teleconference in which any additional feedback or clarifications are documented in meeting minutes.

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

The following forms of FDA feedback to applicants are not considered Pre-Submissions.

Interactions requested by either the applicant or FDA during the review of a marketing application (i.e., following submission of a marketing application, but prior to reaching an FDA Decision).

TPLC Advisory Program Pilot interactions.

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

General questions regarding FDA policy or procedures.

Meetings or teleconferences that are intended to be informational only, including, but not limited to, those intended to educate the review team on new device(s) with significant differences in technology from currently available devices, or to update FDA about ongoing or future product development, without a request for FDA feedback on specific questions related to a planned submission.

Requests for clarification on technical guidance documents, especially where contact is recommended by FDA in the guidance document. However, the following requests will generally need to be submitted as a Pre-Submission in order to ensure appropriate input from multiple reviewers and management: recommendations for device types not specifically addressed in the guidance document; recommendations for nonclinical or clinical studies not addressed in the guidance document; requests regarding use of alternative means to address recommendations specified in a guidance document.

Phone calls or email messages to reviewers that can be readily answered based on a reviewer's experience and knowledge and do not require the involvement of a broader number of FDA staff beyond the routine involvement of the reviewer's supervisor and more experienced mentors.

F. Substantive Interaction

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

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

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

G. Total Time to Decision

Total Time to Decision is the number of calendar days from the date of receipt of an accepted (with respect to 510(k)s) or filed (with respect to Original PMAs and Panel Track Supplements) submission to a MDUFA decision.

For the purpose of calculating and reporting on 510(k) shared outcome Total Time to Decision goals in section II, the average Total Time to Decision for 510(k) submissions is calculated as the average of Total Times to Decision for 510(k) submissions within a 99% closed cohort, with the following provisions:

FY 2023, the cohort excludes submissions with any one hold greater than 180 days and excluding the highest 5% of Total Time to Decision on the remaining cohort.

FY 2024–2027, the cohort excludes the highest 2% and lowest 2% of values and includes all 510(k)s with a MDUFA decision.

In the number of submissions in any MDUFA V receipt cohort exceeds the number of submissions in the FY 2021 or FY 2022 receipt cohort (whichever is higher) by 5% or more, a 1% increase in the trim will be applied to the highest values.

A cohort for a FY is closed when 99% of the MDUFA cohort has reached a MDUFA decision. For the purpose of determining whether improved performance and fee revenue adjustments in Section III are applicable, the 510(k) Shared Outcome Total Time to Decision goal is calculated in the same manner except that the calculation is conducted based on data available as of 18 months following the close of the fiscal year to which the goal applies, and the cohort does not need to be 99% closed. See Section III.

For the purpose of calculating and reporting on PMA shared outcome Total Time to Decision goals in Section II, the average Total Time to Decision for PMAs is calculated as the three-year rolling average of the annual Total Times to Decision for Original PMAs and Panel Track supplements (for example, for FY 2024, the average PMA Total Time to Decision would be the average of FY 2022 through FY 2024) within a closed cohort, excluding the highest 5% and the lowest 5% of values. A cohort for a FY is closed when 95% of the MDUFA V cohort has reached a MDUFA decision. For the purpose of determining whether increased performance and fee revenue adjustments in Section III are applicable, the PMA shared outcome Total Time to Decision goal is calculated in the same manner except that the calculation is conducted based on data available as of 18 months following the close of the fiscal year to which the goal applies and the cohort does not need to be 95% closed.

H. Application Types

Original PMA means an application for an approval of a device submitted under section 515(c) of the FD&C Act. It does not include a

supplement to such an application after it has been approved or a Premarket Report.

Premarket Report means a report submitted under section 515(c)(2) of the FD&C Act seeking premarket approval for a class III reprocessed single use device.

Panel-Track Supplement means a supplement to an approved Original PMA or Premarket Report that requests a significant change in design or performance of the device, or a new indication for use of the device, and for which substantial clinical data are necessary to provide a reasonable assurance of safety and effectiveness.

180-Day PMA Supplement means a supplement to an approved Original PMA or Premarket Report that is not a panel-track supplement and requests a significant change in components, materials, design, specification, software, color additives, or labeling.

Real-Time PMA Supplement means a supplement to an approved Original PMA or Premarket Report that requests a minor change to the device, such as a minor change to the design of the device, software, sterilization, or labeling, and for which the applicant has requested and the agency has granted a meeting or similar forum to jointly review and determine the status of the supplement.

De Novo Classification Request (De Novo Request) means a request made under section 513(f)(2) of the FD&C Act with respect to the classification of a device.

Premarket Notification (510(k)) Submission means a report submitted under section 510(k) of the FD&C Act.

I. BLA-related Definitions

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

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

(a) Final printed labeling

(b) Draft labeling

(c) Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information including important new adverse experiences not previously reported with the product are presented in the resubmission)

(d) Stability updates to support provisional or final dating periods

(e) Commitments to perform Phase 4 studies, including proposals for such studies

(f) Assay validation data

(g) Final release testing on the last 1–2 lots used to support approval

(h) A minor reanalysis of data previously submitted to the application (determined by the Agency as fitting the Class 1 category)

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

(j) Other specific items may be added later as the Agency gains experience with the scheme and will be communicated via guidance documents to industry

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

GDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROGRAM ENHANCEMENTS FISCAL YEARS 2023–2027

GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023–2027

This document contains the performance goals and program enhancements for the Generic Drug User Fee Amendments (GDUFA) reauthorization for fiscal years (FYs) 2023–2027, known as GDUFA III. It is commonly referred to as the ''Goals Letter'' or ''Commitment Letter.'' The Goals Letter represents the product of the Food and Drug Administration's (FDA or the Agency) discussions with the regulated industry and public stakeholders, as mandated by Congress. The performance goals and program enhancements specified in this letter apply to aspects of the generic drug assessment program and build on the GDUFA program established and enhanced through previous authorizations. New enhancements to the program are designed to maximize the efficiency and utility of each assessment cycle, with the intent to reduce the number of assessment cycles for abbreviated new drug applications (ANDAs) and facilitate timely access to quality, affordable, safe and effective generic medicines. Certain new enhancements are specifically designed to foster the development, assessment, and approval of Complex Generic Products. FDA is committed to meeting the performance goals specified in this letter and to continuous improvement of the Agency's performance.

GDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023–2027

The performance goals and procedures of FDA, as agreed to under the third authorization of the generic drug user fee program, are summarized below.

Unless otherwise stated, goals apply to cohorts of each fiscal year. For the purposes of calculating all time periods in this Commitment Letter, FDA will calculate the goal date from the day after a submission, to be consistent with FDA's other user fee programs.

I. SUBMISSION ASSESSMENT PERFORMANCE GOALS

A. Original ANDAs and Amendments

1. Assess and act on 90 percent of standard original ANDAs within 10 months of the date of ANDA submission, subject to any adjustments to the goal dates described in section I(A)(3).

2. Assess and act on 90 percent of priority original ANDAs within the applicable assessment goal, subject to any adjustments to the goal dates described in section I(A)(3).

a. Assess and act on priority original ANDAs within 8 months of the date of ANDA submission if the applicant submits a Pre-Submission Facility Correspondence (PFC) not later than 60 days prior to the date of ANDA submission, and the PFC is found to be complete and accurate, subject to the limitations set forth in section I(A)(2)(b).

b. Assess and act on priority original ANDAs within 10 months of the date of ANDA submission if:

i. the applicant submits a PFC later than 60 days prior to the date of ANDA submission, or does not submit a PFC;

ii. information in a PFC is found to be incomplete or inaccurate;

iii. the information submitted in the ANDA differs significantly from what was submitted in the PFC; or

iv. FDA, upon assessment of a final bioequivalence study report submitted in the ANDA, determines that an inspection of the relevant site or sites is necessary.

3. If, upon initial submission, a standard or priority original ANDA contains a certification that a site/facility listed on the Form FDA 356h is not ready for inspection (i.e., the box ''no'' is checked in response to ''is the site ready for inspection?'' in section 28), FDA will set a goal date that is 15 months from the date of submission. FDA will conduct a filing review of such an ANDA but will not commence substantive assessment of the application until an amendment described in subsection I(A)(3)(a) is submitted, or the goal date is reset pursuant to I(A)(3)(b).

a. During the initial 15-month review period, if the applicant submits an amendment with a Form FDA 356h that certifies all facilities are ready for inspection, FDA will set a new goal date that is 8 months from the

date of submission for priority amendments (if a PFC was submitted per I(A)(2)(a)), or 10 months from the date of submission for other amendments.

b. If the applicant does not submit an amendment described in I(A)(3)(a) by 30 days before the goal date, FDA will reset the goal date for an additional 15 months, i.e., 30 months from the date of original ANDA submission. FDA will assess and act on 90 percent of such ANDAs within 30 months of the date of the original submission as applicable.

4. Assess and act on 90 percent of standard Major Amendments within the applicable assessment goal.

a. Assess and act on standard Major Amendments within 8 months of the date of amendment submission if preapproval inspection is not required.

b. Assess and act on standard Major Amendments within 10 months of the date of amendment submission if preapproval inspection is required.

5. Assess and act on 90 percent of priority Major Amendment submissions within the applicable assessment goal.

a. Assess and act on priority Major Amendments within 6 months of the date of amendment submission if preapproval inspection is not required.

b. Assess and act on priority Major Amendments within 8 months of amendment submission if a preapproval inspection is required, the applicant submits a PFC not later than 60 days prior to the date of amendment submission, and the PFC is found to be complete and accurate, subject to the limitations set forth in section I(A)(6).

6. Assess and act on priority Major Amendments within 10 months of amendment submission if a preapproval inspection is required and if:

a. the applicant submits a PFC later than 60 days prior to the date of the amendment, or does not submit a PFC;

b. information in a PFC is found to be incomplete or inaccurate;

c. the information submitted in the amendment differs significantly from what was submitted in the PFC; or

d. FDA, upon assessment of a final bioequivalence study report submitted in the amendment, determines that an inspection of the relevant site or sites is necessary.

7. Assess and act on 90 percent of standard and priority Minor Amendments within 3 months of the date of amendment submission.

TABLE FOR SECTION I(A)(1) AND (2): ORIGINAL ANDAs

Submission Type	Goal
Standard Original ANDAs.	90% within 10 months of submission date, subject to any adjustment to the goal date described in section I(A)(3).
Priority Original ANDAs.	90% within 8 months of submission date if applicant meets requirements under section I(A)(2)(a), subject to any adjustment to the goal date described in section I(A)(3). 90% within 10 months of submission date if applicant meets any limitations as described under section I(A)(2)(b), subject to any adjustment to the goal date described in section I(A)(3).

TABLE FOR SECTION I(A)(4)–(7): AMENDMENTS

Submission Type	Goal
Standard Major Amendments.	90% within 8 months of submission date if preapproval inspection not required. 90% within 10 months of submission date if preapproval inspection required.
Priority Major Amendments.	90% within 6 months of submission date if preapproval inspection not required. 90% within 8 months of submission date if preapproval inspection required and applicant meets requirements under section I(A)(5)(b). 90% within 10 months of submission date if preapproval inspection required and applicant meets any limitations as described under section I(A)(6).
Standard and Priority Minor Amendments.	90% within 3 months of submission date.

B. PASs and PAS Amendments

1. Assess and act on 90 percent of standard prior approval supplements (PASs) within the applicable assessment goal.

a. Assess and act on standard PASs within 6 months of the date of PAS submission if preapproval inspection is not required.

b. Assess and act on standard PASs within 10 months of the date of PAS submission if preapproval inspection is required.

2. Assess and act on 90 percent of priority PASs within the applicable assessment goal.

a. Assess and act on priority PASs within 4 months of the date of PAS submission if preapproval inspection is not required.

b. Assess and act on priority PASs within 8 months of the date of PAS submission if a preapproval inspection is required, the applicant submits a PFC not later than 60 days prior to the date of PAS submission, and the PFC is found to be complete and accurate, subject to the limitations set forth in section I(B)(2)(c).

c. Assess and act on priority PASs within 10 months of PAS submission if a preapproval inspection is required and if:

i. the applicant submits a PFC later than 60 days prior to the date of PAS submission, or does not submit a PFC;

ii. information in a PFC is found to be incomplete or inaccurate;

iii. the information submitted in the PAS differs significantly from what was submitted in the PFC; or

iv. FDA, upon assessment of a final bioequivalence study report submitted in the PAS, determines that an inspection of the relevant site or sites is necessary.

3. Assess and act on 90 percent of Major Amendments to standard PASs within the applicable assessment goal.

a. Assess and act on Major Amendments to standard PASs within 6 months of the date of amendment submission if preapproval inspection is not required.

b. Assess and act on Major Amendments to standard PASs within 10 months of the date of amendment submission if preapproval inspection is required.

4. Assess and act on 90 percent of Major Amendments to priority PASs within the applicable assessment goal.

a. Assess and act on Major Amendments to priority PASs within 4 months of the date of amendment submission if preapproval inspection is not required.

b. Assess and act on priority Major Amendments to priority PASs within 8 months of amendment submission if a preapproval inspection is required, if the applicant submits a PFC not later than 60 days prior to the date of amendment submission, and the PFC is found to be complete and accurate, subject to the limitations set forth in section I(B)(4)(c).

c. Assess and act on priority Major Amendments to priority PASs within 10 months of amendment submission if a preapproval inspection is required and if:

i. the applicant submits a PFC later than 60 days prior to the date of the PAS amendment, or does not submit a PFC;

ii. information in a PFC is found to be incomplete or inaccurate;

iii. the information submitted in the PAS amendment differs significantly from what was submitted in the PFC; or

iv. FDA, upon assessment of a final bioequivalence study report submitted in the amendment, determines that an inspection of the relevant site or sites is necessary.

5. Assess and act on 90 percent of Minor Amendments to standard and priority PASs within 3 months of the date of amendment submission.

TABLE FOR SECTION I(B)(1) AND (2): PASs

Submission Type	Goal
Standard PASs	90% within 6 months of submission date if preapproval inspection not required. 90% within 10 months of submission date if preapproval inspection required.
Priority PASs	90% within 4 months of submission date if preapproval inspection not required. 90% within 8 months of submission date if preapproval inspection required and applicant meets requirements under section I(B)(2)(b). 90% within 10 months of submission date if preapproval inspection required and applicant meets any limitations as described under section I(B)(2)(c).

TABLE FOR SECTION I(B)(3)–(5): PAS AMENDMENTS

Submission Type	Goal
Standard PAS Major Amendments.	90% within 6 months of submission date if preapproval inspection not required. 90% within 10 months of submission date if preapproval inspection required.
Priority PAS Amendments.	90% within 4 months of submission date if preapproval inspection not required. 90% within 8 months of submission date if preapproval inspection required and applicant meets requirements under section I(B)(4)(b). 90% within 10 months of submission date if preapproval inspection required and applicant meets any limitations as described under section I(B)(4)(c).
Standard and Priority Minor PAS Amendments.	90% within 3 months of submission date.

C. Unsolicited Amendments and PAS Amendments

1. Assess and act on Unsolicited Amendments and PAS amendments submitted during the assessment cycle by the later of the goal date for the original submission/solicited amendment or the goal date assigned in accordance with sections (I)(A)(4), (5), (6) and (7) and (I)(B)(3), (4) and (5), respectively, for the Unsolicited Amendment.

2. Assess and act on Unsolicited ANDA Amendments and PAS amendments submitted between assessment cycles by the later of the goal date for the subsequent solicited amendment or the goal date assigned in accordance with sections (I)(A)(4), (5), (6), and (7) and (I)(B)(3), (4), and (5), respectively, for the Unsolicited Amendment.

D. Drug Master Files (DMFs)

Complete the initial completeness assessment for 90 percent of Type II active pharmaceutical ingredient (API) DMFs within 60 days of the later of the date of DMF submission or DMF fee payment.

TABLE FOR SECTION I(D): DMFs

Submission Type	Goal
Type II API DMF ...	90% of initial completeness assessments within 60 days of the later of the date of DMF submission or DMF fee payment.

E. Controlled Correspondence

1. A Controlled Correspondence may be submitted by or on behalf of a generic drug manufacturer or related industry prior to ANDA submission. Under the GDUFA II framework, correspondence seeking regulatory and/or scientific advice after issuance of a Complete Response Letter (CRL) or tentative approval, or after ANDA approval, was considered general correspondence. Under GDUFA III, these types of correspondence can be submitted as Controlled Correspondence. During an ANDA assessment cycle, a Controlled Correspondence may only be submitted if an applicant seeks further feedback from FDA after a product-specific guidance (PSG) Teleconference, as described in section III(C)(5)(c), below, or to seek a Covered Product Authorization. During an ANDA assessment cycle, all other correspondence will be general correspondence.

2. Review and respond to 90 percent of Controlled Correspondence within the applicable review goal.

a. Review and respond to Level 1 Controlled Correspondence within 60 days of the date of submission.

b. Review and respond to Level 2 Controlled Correspondence within 120 days of the date of submission.

3. FDA will review and respond to 90 percent of submitter requests to clarify ambiguities in the Controlled Correspondence response within 21 days of receipt of the request. The response to the submitter's request will provide clarification or advice concerning the ambiguity in the Controlled Correspondence response.

TABLE FOR SECTION I(E): CONTROLLED CORRESPONDENCE

Submission Type	Goal
Level 1 Controlled Correspondence.	90% within 60 days of submission date.
Level 2 Controlled Correspondence.	90% within 120 days of submission date.

FDA will review and respond to 90% of submitter requests to clarify ambiguities in the Controlled Correspondence response within 21 days of request receipt.

II. ORIGINAL ANDA ASSESSMENT PROGRAM ENHANCEMENTS

A. ANDA Receipt

1. FDA will strive to determine whether to receive ANDAs within 60 days of the date of ANDA submission.

2. To enable FDA to rapidly determine whether to receive an ANDA pursuant to 21 CFR 314.101, and with consideration of final Agency guidances that address ANDA receipt determinations, FDA will communicate minor technical deficiencies (e.g., document legibility) and deficiencies potentially resolved with information in the ANDA at original submission within 10 days of original ANDA submission. If a deficiency is resolved within 10 days, that deficiency will not be a basis for a refuse-to-receive decision.

3. At the time of receipt, FDA will notify the applicant in the acceptance letter whether the ANDA or PAS is subject to priority or standard assessment.

B. ANDA Assessment Transparency and Communications Enhancements

To promote transparency and communication between FDA and ANDA applicants, FDA will apply the assessment program enhancements below to the assessment of all ANDAs. The goal of these program enhancements is to improve predictability and transparency, promote the efficiency and effectiveness of the review process, minimize the number of assessment cycles necessary for approval, increase the overall rate of approval, and facilitate greater access to generic drug products.

1. Information Requests (IRs) and Discipline Review Letters (DRLs):

a. IRs and DRLs do not stop the assessment clock.

b. In the first assessment cycle, FDA will issue the appropriate IR(s) and/or DRL(s) from each assessment discipline by the midpoint of the assessment, with the exception of the Labeling discipline as described in subsection II(B)(2) below.

i. In a Mid-Cycle DRL, the assessment discipline will assign a due date for response and identify major and minor deficiencies.

ii. If an applicant responds by the response due date, FDA will assess a response to minor deficiencies within the originally assigned goal date for the submission, subject to the exceptions described in II(B)(1)(iii).

iii. Responses to any major deficiencies, or to minor deficiencies that include data and information that require comparable FDA assessment resources to those required for major deficiencies, for example, a consult, will be considered Major Amendments. FDA will extend the goal date consistent with the number of months needed to assess a comparable standard or priority Major Amendment (see section I(A)(4)–(6)).

c. FDA will issue IRs and DRLs after the midpoint of the first assessment cycle and at any time in subsequent assessment cycles, when, in FDA's judgment, there are one or more minor deficiencies in a discipline that, if resolved using an IR or DRL, could lead to approval or tentative approval of an ANDA in the current assessment cycle. FDA will issue the IR or DRL and provide a due date for the applicant's response before the goal date.

i. If the applicant responds to the minor deficiencies in the IR or DRL by the due date, and FDA finds the amendment to satisfactorily address all of the issues identified in the IR or DRL, and the response does not contain unsolicited information, FDA may extend the goal date by 90 days from the date of the applicant's response.

ii. FDA's decision to extend the goal date will be communicated in an amendment acknowledgement letter.

iii. FDA will continue to issue IRs and/or DRLs late in the assessment cycle for original submissions and amendments until it is no longer feasible within the current assessment cycle for the applicant to develop and FDA to assess a response to the IR and/or DRL. For IRs and DRLs issued past the midpoint of the assessment cycle, the assessment discipline generally will assign a due date for response and identify major and minor deficiencies. DRLs issued without a response due date likely will signify a forthcoming CRL.

d. If the applicant does not provide a complete response to an IR and/or DRL by the response due date (or any agreed-upon extension), FDA may include the same deficiencies from the IR or DRL in a CRL and assess the response during the next assessment cycle.

e. If a discipline identifies a Significant Major deficiency, that deficiency will be communicated in a CRL as soon as is feasible.

2. Specific commitments related to IRs and DRLs for labeling:

a. In the first assessment cycle, the Labeling Discipline will:

i. upon receiving an ANDA for assessment, make an initial determination whether there is a need for a consult to be issued to another review discipline, including for a consult regarding an applicant's request to ''carve out'' language in the proposed labeling protected by patents or exclusivities, and will initiate such consults;

ii. strive to issue any DRL at approximately months 6–7 of the assessment for those ANDAs with a 10-month goal date, or months 5–6 of the assessment for those ANDAs with an 8-month goal date, with the exception that there may be a delay of the issuance of any labeling deficiencies that result from changes to the labeling of the reference listed drug (RLD) or a new exclusivity or patent listing;

iii. limit the assessment of labeling to one IR/DRL if other disciplines will not be acceptable during the first cycle; and

iv. continue to assess labeling to enable an action within the assessment cycle if other disciplines are acceptable.

b. Labeling IRs and DRLs in all assessment cycles:

FDA will minimize issuing CRLs that contain only labeling deficiencies by, for example, utilizing later-cycle IRs and the imminent action process.

3. Imminent Actions:

a. FDA will continue assessment of an ANDA past the goal date if, in FDA's judgment, it may be possible to approve or tentatively approve an ANDA within 60 days after the goal date. Such circumstances may include:

i. When the application meets the requirements for tentative approval by the goal date, but the legally permissible ANDA approval date is within 60 days after the goal date, and FDA may be able to approve the ANDA when it becomes legally permissible to do so.

ii. When FDA may be able to approve or tentatively approve an application submitted by a first applicant by the 30-month forfeiture date described in section 505(j)(5)(D)(i)(IV) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)(5)(D)(i)(IV)).

iii. When, at the sole discretion of FDA, and subject to resources, one or more small issues remain from one or more disciplines that in FDA's judgment may be resolved within 60 days after the goal date.

b. If an ANDA is approved or tentatively approved within 60 days after the goal date, the goal date will be considered to have been met.

4. FDA will strive to act prior to a goal date, or the 60-day period for an imminent action, when the assessment is complete and there are no outstanding deficiencies.

5. To facilitate the labeling assessment, an applicant will clearly state in the cover letter to an ANDA, amendment, PAS, or PAS Amendment that the submission includes a proposed labeling carve-out.

6. Communication regarding Deficiencies and Actions:

a. With respect to imminent actions, applicants may inquire and FDA will promptly respond to an applicant inquiry seeking information as to whether FDA intends to work through the goal date in accordance with section II(B)(3). This communication will be preliminary and subject to change.

b. If a regulatory project manager (RPM) learns that a major deficiency is likely forthcoming, the RPM will notify the applicant. The RPM will not be expected to discuss the nature of the specific forthcoming deficiencies prior to issuance of the CRL.

c. If an RPM learns that FDA is likely to miss the goal date for an ANDA, the RPM will notify the applicant of the delay in taking an action, identify the general reason for the delay including the outstanding discipline(s), if any, and the estimated time for FDA's action on the application.

d. The applicant may periodically request a Review Status Update for each discipline. In response to the applicant's request, the RPM will timely provide a Review Status Update for each discipline.

7. FDA will indicate the assessment classification for a responding amendment in a CRL and include FDA's basis for classifying a responding amendment as Major.

8. Applicants who receive a CRL have the following options with respect to engaging with FDA prior to responding to the CRL:

a. A post-CRL teleconference to seek clarification concerning deficiencies identified in a CRL. FDA will grant appropriate requests for teleconferences requested by applicants upon receiving first-cycle CRLs and upon receiving subsequent CRLs. An appropriate request is one that clearly identifies the specific deficiencies to be discussed and the reason why such deficiencies are not clear. FDA will provide a scheduled date for 90 percent of post-CRL teleconferences within 14 days of the request for a teleconference and conduct 90 percent of such post-CRL teleconferences, if granted, within 30 days of receipt of the written request;

b. Submission of a Controlled Correspondence as described in section I(E); or

c. A post-CRL Scientific Meeting to request scientific advice on possible approaches to address deficiencies identified in

a CRL related to establishing equivalence, subject to the conditions described in section IV(C).

C. Assessment Classification Changes During the Assessment Cycle

1. If during the assessment of an ANDA, ANDA amendment, PAS, or PAS amendment, the assessment classification changes from Standard to Priority, FDA will notify the applicant within 14 days of the date of the change.

2. An applicant may request a change in the assessment classification at any time during the assessment.

3. Once an ANDA or PAS submission is classified as being subject to priority assessment, the application will retain such priority assessment classification status for the duration of that assessment cycle.

4. FDA will include an explanation of the reasons for any denial of an assessment status reclassification request.

5. If an applicant requests a teleconference as part of its request to reclassify a Major Amendment or standard assessment status, FDA will schedule and conduct the teleconference and decide 90 percent of such reclassification requests within 30 days of the date of FDA's receipt of the request for a teleconference. This goal only applies when the applicant accepts the first scheduled teleconference date offered by FDA. This goal does not apply to a Major Amendment in response to a CRL that was deemed major only due to a facility deficiency (''Facility-Based Major CRL Amendment'') described in section II(C)(7).

6. An amendment in response to a CRL classified by FDA as Minor that is submitted more than one year after the date FDA issued the CRL will be reclassified as a Major Amendment, except for ANDAs for products that are on the drug shortage list under section 506E of the FD&C Act (21 U.S.C. 356e), or are the subject of a response to a Public Health Emergency as declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the Public Health Service Act (PHS Act) (42 U.S.C. 247d), or are anticipated to be subject to the same criteria as apply to such a declaration, at the time of submission.

7. Reclassification of Facility-Based Major CRL Amendments

a. Upon submission of a Facility-Based Major CRL Amendment, an applicant can request that FDA reclassify the Major Amendment to minor.

b. A request for reclassification must be made at the time of amendment submission and include supporting information detailing why the facility deficiency has been resolved and no additional facility assessment is needed.

c. FDA will grant the request to reclassify the Facility-Based Major CRL Amendment if FDA determines that none of the following are necessary to complete the assessment of the amendment:

i. A facility inspection

ii. Use of alternate tools for facility assessment

iii. Continued assessment of inspection deficiency responses

d. If FDA denies the request, the Agency will communicate the substantive basis of the denial to the applicant and the ANDA amendment will be assigned a 6-, 8- or 10-month goal date, as applicable, from the original date of the amendment submission.

e. FDA will make a decision on a request for reclassification of a Facility-Based Major CRL Amendment within 30 days from the date of submission for priority amendments, and within 60 days from the date of submission for standard amendments. If the Facility-Based Major CRL Amendment is reclassified as minor, the goal date will be 3 months from the end of the 30- or 60-day decisional period, as applicable.

f. The goal dates for decisions on requests for reclassification and amendment assessment for which a request for reclassification is submitted are as follows:

Submission Type	FDA Response Regarding Major to Minor Reclassification	New ANDA Goal Date if Reclassification Granted	ANDA Goal Date if Reclassification Denied
Standard Major Amendment	Within 60 days of submission date	Within 5 months of submission date	Within 8 months of submission date if preapproval inspection is not required. Within 10 months of submission date if preapproval inspection is required.
Priority Major Amendment	Within 30 days of submission date	Within 4 months of submission date	Within 6 months of submission date if preapproval inspection is not required. Within 8 months of submission date if preapproval inspection required and applicant meets the requirements under section I(A)(5)(b). Within 10 months of submission date if preapproval inspection required and applicant meets any limitations as described under section I(A)(6).

D. ANDA Approval and Tentative Approval

If applicants submit and maintain ANDAs consistent with the statutory requirements for approval under 505(j) of the FD&C Act; respond to IRs and DRLs completely and within the time frames requested by FDA; and timely submit all required information under 21 CFR parts 314 and 210, including information concerning notice (21 CFR 314.95), litigation status (21 CFR 314.107), and commercial marketing (21 CFR 314.107); then FDA will strive to:

1. Approve approvable ANDAs in the first assessment cycle;

2. Approve First Generics on the earliest lawful approval date, if known to FDA; and

3. Tentatively approve or approve ANDAs for ''First Applicants'' as described in section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act to avoid forfeiture of 180-day exclusivity.

E. Dispute Resolution

1. An applicant may pursue a request for reconsideration within the assessment discipline at the Division level or original signatory authority, as needed.

2. The Office of Generic Drugs, Office of Regulatory Operations Associate Director will track each request for Division-level reconsideration through resolution.

3. Following resolution of a request for reconsideration, an applicant may pursue formal dispute resolution above the Division level, pursuant to procedures set forth in Formal Dispute Resolution: Sponsor Appeals Above the Division Level Guidance for Industry and Review Staff (May 2019).

4. FDA will respond to 90 percent of appeals above the Division level within 30 days of CDER's receipt of the written appeal.

5. CDER's Formal Dispute Resolution Project Manager (or designee) will track each formal appeal above the Division level through resolution.

F. Pre-Submission Facility Correspondence

1. For the purposes of section I.A. and I.B. above, FDA will consider a PFC to be complete and accurate if the submission consists of the following:

a. For each manufacturing and testing facility involved in manufacturing processes and testing for the ANDA and corresponding Type II API DMF:

i. facility name, operation(s) performed, facility contact name, address, FDA Establishment Identifier (FEI) number (if a required registrant or one has been assigned), DUNS number, registration information (for required registrants), and a confirmation that the facility is ready for inspection,

ii. information needed to inform FDA's decision regarding the need for a preapproval inspection, such as a description of the manufacturing process and controls of critical steps, identification of any anticipated differences between pilot/exhibit scale and commercial scale processes, and as otherwise described in the guidance for industry on ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications (Pre-Submission Facility Correspondence) (November 2017) and any revisions, and

iii. a certification by the applicant that any Type II DMF has similarly complete and accurate facility information, including complete facility information (i.e., facility name, operation, facility contact name, address, FEI number and DUNS number, and a confirmation that the facility is ready for inspection).

b. Information needed to inform FDA's decision regarding the need for a preapproval inspection, such as a description of the drug substance manufacturing process, that is included in a corresponding Type II DMF is not required to be duplicated in the PFC for the ANDA if it is included in a corresponding Type II DMF.

c. For all sites or organizations involved in all bioequivalence and clinical studies used to support the ANDA submission: site names, addresses, and website; the study numbers; a list and description of all study investigators consistent with the guidance ICH E3 Structure and Content of Clinical Study Reports (July 1996) section 16.1.4; the study conduct dates; and study protocols and any available amendments.

d. For all sites or organizations involved in analytical studies used to support the ANDA application submission the following are required: analytical site name, address, and website. For those studies that were initiated no later than 60 days prior to the ANDA submission, additional requirements are:

i. a list of investigator name(s)

ii. study conduct dates; and

iii. if the analytical method validation was completed before dosing, the analytical method validation study report(s).

e. This information is provided using a standardized electronic format and includes unique identifiers that are current and accurate.

2. Changes to information contained in a PFC when submitted in an ANDA that are considered a ''significant change'' include changes in the identified facilities for manufacture of the drug substance or drug product, the proposed manufacturing operations or operating principles, and the order of manufacturing unit operations, as described in the guidance ANDAs: Pre-Submission of

Facility Information Related to Prioritized Generic Drug Applications (Pre-Submission Facility Correspondence) (November 2017) and any revisions.

G. Other ANDA Assessment Program Aspirations

1. FDA aspires to continually improve the efficiency of the ANDA Assessment program.

2. The absence of a GDUFA III commitment for a specific program function does not imply that the program function is not important. For example, other program functions include determining whether listed drugs were voluntarily withdrawn from sale for reasons of safety or effectiveness and ANDA proprietary name evaluations.

III. PRE-ANDA PROGRAM

A. Goal of Pre-ANDA Program

1. The goal of the pre-ANDA program is to clarify regulatory expectations for prospective applicants early in product development, assist applicants in developing more complete submissions, promote a more efficient and effective ANDA assessment process, and reduce the number of assessment cycles required to obtain ANDA approval.

2. Some elements of these programs are tailored to enhance the development of Complex Generic Products. Complex Generic Products can raise unique scientific and regulatory considerations, and FDA is committed to providing further transparency and clarity on Complex Generic Product development and assessment to help increase the availability of these products.

B. Suitability Petitions

1. In FY 2023, FDA will work diligently to enhance the Agency's processes for reviewing and responding to petitions submitted under section 505(j)(2)(C) of the FD&C Act (commonly referred to as ''suitability petitions''), and to review and respond to pending suitability petitions.

2. Prior to FY 2024, FDA will take appropriate action to determine if petitioners who submitted suitability petitions prior to FY 2023 remain interested in a response.

3. FDA will conduct a completeness assessment for suitability petitions submitted in FY 2024–2027. The timeframe for the completeness assessment will be:

a. 21 days after the date of petition submission; or

b. If an IR is issued as part of the completeness assessment and the petitioner submits a response, FDA will finish the completeness assessment within 21 days after the date of receipt of the IR response.

4. Any suitability petition submitted in FY 2024–2027 will receive a goal date described in section III(B)(7). Any suitability petitions submitted to FDA prior to FY 2024 will not receive a goal date. If a petitioner wants to receive a goal date on a suitability petition submitted prior to FY 2024, the petitioner may withdraw and submit a new suitability petition in FY 2024–2027.

5. The date of submission for the purposes of determining the fiscal year of submission will be the date of FDA's completion of the completeness assessment.

6. FDA will prioritize the review of suitability petitions for a drug product that:

a. could mitigate or resolve a drug shortage and prevent future shortages;

b. address a public health emergency declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the PHS Act, or anticipated under the same criteria as apply to such a declaration;

c. is for a new strength of a parenteral product that could aid in eliminating pharmaceutical waste or mitigating the number of vials needed per dose by addressing differences in patient weight, body size, or age; or

d. is subject to special review programs under the President's Emergency Plan for AIDS Relief (PEPFAR).

7. Beginning in FY 2024, FDA will review and respond to suitability petitions that have been assigned a goal date pursuant to the following goals:

a. In FY 2024, 50 percent of submissions within 6 months after completeness assessment, up to a maximum of 50 suitability petitions completed;

b. In FY 2025, 70 percent of submissions within 6 months after completeness assessment, up to a maximum of 70 suitability petitions completed;

c. In FY 2026, 80 percent of submissions within 6 months after completeness assessment, up to a maximum of 80 suitability petitions completed; and

d. In FY 2027, 90 percent of submissions within 6 months after completeness assessment, up to a maximum of 90 suitability petitions completed.

8. As a general matter, if FDA misses goal dates on suitability petitions due to increased submissions, FDA will prioritize the review of suitability petitions for which a goal date was missed prior to reviewing newly submitted suitability petitions for the current fiscal year, except for those suitability petitions that are prioritized under section III(B)(6). See Appendix for additional information on FDA's review of suitability petitions in GDUFA III.

C. Product-Specific Guidance

1. FDA will continue to issue PSG identifying the methodology for generating evidence needed to support ANDA approval.

2. FDA will issue PSGs consistent with the following goals:

a. For Complex Products approved in new drug applications (NDAs) on or after October 1, 2022, a PSG will be issued for 50 percent of such NDA products within 2 years after the date of approval, and for 75 percent of such NDA products within 3 years after the date of approval.

b. FDA will continue to develop PSGs for Complex Products approved prior to October 1, 2022, for which no PSG has been published.

c. For non-complex drug products approved in NDAs on or after October 1, 2022, that contain a new chemical entity (NCE) (as described in section 505(j)(5)(F)(ii) of the FD&C Act), a PSG will be issued within 2 years after the date of approval for 90 percent of such products.

3. Information on PSG Development:

a. FDA will provide on its website information related to upcoming new and revised PSGs to support the development and approval of safe and effective generic drug products, including the projected date of PSG publication, which may be subject to change. When FDA becomes aware that it will not meet the issuance date listed on the website, FDA will update the website to provide a new projected issuance date in the next scheduled update.

b. FDA routinely will update the information on this website approximately every 4 months.

c. PSGs will be developed (or revised) and issued in accordance with FDA's Good Guidance Practices and will be reviewed by senior management and other designated subject matter experts prior to publication and after consideration of any public comments submitted to the relevant docket of a published draft or final PSG.

4. Prioritization of PSG Development:

a. FDA will make available on its website information on how the Agency prioritizes the development of PSGs.

b. Industry may request via the portal for Controlled Correspondence that FDA develop a PSG. FDA will consider this request in prioritizing PSG development but will not consider this to be a Controlled Correspondence.

c. FDA will seek public input on prioritization of PSGs annually during the public meeting on research prioritization described in section V(B)(2).

d. For Complex Products, FDA generally will prioritize the development of PSGs for Complex Products that contain a NCE (as described in section 505(j)(5)(F)(ii) of the FD&C Act) over Complex Products that do not contain an NCE.

5. When a new or revised PSG is published and an applicant or prospective applicant has already commenced an in vivo bioequivalence study (i.e., the study protocol has been signed by the study sponsor and/or the contract research organization) the applicant or prospective applicant may request a PSG Teleconference to obtain Agency feedback on the potential impact of the new or revised PSG on its development program.

a. To be eligible for a PSG Teleconference, the applicant or prospective applicant must submit with the meeting request the signature page of the relevant in vivo study protocol signed by the study sponsor and/or the contract research organization.

b. FDA will hold a PSG Teleconference within 30 days after the receipt of the meeting request. The PSG Teleconference will be scheduled for 60 minutes.

c. If the applicant seeks further feedback from FDA after a PSG Teleconference, the applicant may utilize the Controlled Correspondence process or request an additional meeting. The purpose of this meeting is to provide a forum in which industry can discuss the scientific rationale for an approach other than the approach recommended in the PSG to ensure that the approach complies with the relevant statutes and regulations.

i. If the applicant has not submitted an ANDA, the prospective applicant can submit a request for a Pre-Submission PSG Meeting. FDA will grant or deny the meeting within 14 days after receipt of the request and if granted, will schedule the meeting within 120 days after receipt of the request.

ii. If the applicant has submitted an ANDA, the applicant can submit a request for a Post-Submission PSG Meeting. FDA will grant or deny the meeting within 14 days after receipt of the request, and if granted, will schedule the meeting within 90 days after receipt of the request.

iii. FDA may deny a Pre- or Post-Submission PSG Meeting if the request is incomplete, or the inquiry would be more appropriately resolved through a Controlled Correspondence. FDA may grant a Pre- or Post-Submission Meeting request after such a Controlled Correspondence if the Agency determines that any issue(s) remain unresolved or would be more appropriately resolved in a meeting.

iv. Applicants and prospective applicants are eligible to request a Pre-Submission PSG Meeting or Post-Submission PSG Meeting regardless of whether they have had a Product Development Meeting or a post-CRL Scientific Meeting.

6. When FDA intends to issue a new or revised PSG and there are ANDAs under review that may be impacted by changes to the new or revised PSG, FDA will ensure that at least division-level program leadership is aware of the potential impact on the pending ANDAs for drug products with related new or revised PSGs.

D. Product Development Meetings

1. A prospective applicant can request a pre-ANDA submission Product Development Meeting. The purpose of the meeting is to provide a forum for a scientific exchange on specific issues (e.g., a proposed study design,

alternative approach, additional study expectations, or questions) in which FDA will provide targeted advice regarding an ongoing ANDA development program.

2. FDA will grant a prospective applicant a Product Development Meeting if, in FDA's judgment:

a. The requested Product Development Meeting concerns:

i. Development of a Complex Generic Product for which FDA has not issued a PSG; or

ii. An alternative equivalence evaluation, i.e., change in study type, such as in vitro to clinical, for a Complex Generic Product for which FDA has issued a PSG;

b. The prospective applicant submits a complete meeting package, including a data package and specific proposals;

c. A Controlled Correspondence response would not adequately address the prospective applicant's questions; and

d. A Product Development Meeting would significantly improve ANDA assessment efficiency.

3. Dependent on available resources, FDA may grant a prospective applicant a Product Development Meeting concerning development issues other than those described in Section III(D)(2) if, in FDA's judgment:

a. The prospective applicant submits a complete meeting package, including a data package and specific proposals;

b. A Controlled Correspondence response would not adequately address the prospective applicant's questions; and

c. A Product Development Meeting would significantly improve ANDA assessment efficiency.

4. FDA will grant or deny 90 percent of Product Development Meeting requests within 14 days after receipt of the meeting request.

5. FDA will conduct 90 percent of Product Development Meetings within 120 days after the meeting is granted.

6. FDA can meet the Product Development Meeting goal by either conducting a meeting or providing a meaningful written response that will inform drug development and/or regulatory decision-making to the prospective applicant, within the applicable goal date.

7. Unless FDA is providing a written response to satisfy the Product Development Meeting goal, FDA will provide preliminary written comments before each Product Development Meeting (and aspire to provide the written comments 5 days before the meeting) and will provide meeting minutes within 30 days following the meeting.

E. Pre-Submission Meetings

1. Prospective applicants may request a Pre-Submission Meeting. The purpose of a Pre-Submission Meeting is to provide an applicant the opportunity to present unique or novel data or information that will be included in the ANDA submission such as formulation, key studies, justifications, and/or methods used in product development, as well as the interrelationship of the data and information in the ANDA. FDA will grant a Pre-Submission Meeting, if the applicant was granted a Product Development Meeting for the same Complex Generic Product or FDA believes in its sole discretion that the Pre-Submission Meeting would improve assessment efficiency.

2. For Pre-Submission Meetings, FDA will:

a. Identify the ANDA assessment team members who will attend the meeting;

b. I entify additional content for the meeting in the letter granting the meeting request, including information on what topics should be addressed in the meeting in addition to those identified in the meeting request by the applicant; and

c. Identify at the meeting, items or information for clarification before the applicant's submission of the ANDA.

3. FDA will not provide a substantive assessment of summary data or full study reports at the meeting.

4. An applicant's decision not to request a Pre-Submission Meeting will not prejudice the receipt or assessment of an ANDA.

5. FDA will grant or deny 90 percent of Pre-Submission Meeting requests within 30 days.

6. If. granted, FDA will conduct 90 percent of Pre-Submission Meetings within 60 days of the meeting request.

7. FDA will provide preliminary written comments 5 days before each meeting, and meeting minutes within 30 days after the meeting.

IV. ANDA ASSESSMENT MEETING PROGRAM

A. Goal of the ANDA Assessment Meeting Program

1. The goal of the ANDA Assessment Meeting Program is to provide or continue to provide targeted, robust advice to ANDA applicants as they work to meet the standards for ANDA approval.

2. Some elements of this program are tailored to enhance the development of Complex Generic Products.

B. Mid-Cycle Review Meetings and Enhanced Mid-Cycle Review Meetings

1. If an applicant for a Complex Generic Product was granted a Product Development Meeting for the same product, they may, within 7 days of receiving the last mid-Cycle DRL, submits a request for a Mid-Cycle Review Meeting or an Enhanced Mid-Cycle Meeting. The request should describe the specific deficiency(ies) to be discussed.

2. Mid-Cycle Review Meetings:

a. The purpose of a Mid-Cycle Review Meeting is for the applicant to ask for the rationale for any deficiency identified in the mid-cycle DRL(s), and/or to ask questions related to FDA's assessment of the data or information in the ANDA. An applicant may not present any new data or information at this meeting.

b. The Mid-Cycle Review Meeting will take place within 30 days after the date the sponsor submits a meeting request.

3. Enhanced Mid-Cycle Review Meetings:

a. The purpose of this meeting is for the applicant to ask questions related to a proposed scientific path to address possible deficiencies identified in the mid-cycle DRL(s). An applicant may ask questions about potential new data or information to address any possible deficiencies identified in the mid-cycle DRL(s). FDA will discuss the data and information but will not provide substantive assessment of data or information provided by the applicant at the meeting.

b. If an Enhanced Mid-Cycle Review Meeting is requested, the meeting will take place within 90 days after issuance of the last mid-cycle DRL.

c. FDA will extend the ANDA goal date by 60 days if an applicant requests an Enhanced Mid-Cycle Review Meeting. FDA also will extend the response due date for the relevant DRL(s) by recalculating the response due date starting from the date of the meeting, e.g., if the response was due 30 days after the DRL was issued, it will now be due 30 days after the Enhanced Mid-Cycle Review Meeting.

d. An applicant may submit an Unsolicited Amendment after an Enhanced Mid-Cycle Review Meeting, which could result in an additional goal date extension consistent with section I(C).

C. Post-CRL Scientific Meetings

1. An applicant can request a Post-CRL Scientific Meeting. The purpose of this meeting is to provide an applicant scientific advice on possible approaches to address deficiencies identified in a CRL related to establishing equivalence.

a. An applicant's meeting request must discuss:

iii. a new equivalence study needed to address the deficiencies in the design identified in the CRL,

iv. an approach that is different from that submitted in the ANDA, e.g., a change in study type from in vivo to in vitro,

v. a new comparative use human factors study, or

vi. a new approach to demonstrating sameness of a complex active ingredient; and

b. FDA will grant the meeting if it is for a Complex Generic Product or in FDA's judgment the request raises issues that are best addressed via this meeting process and cannot be adequately addressed through Controlled Correspondence.

c. An applicant may have a post-CRL teleconference described in section II(B)(8)(a) prior to requesting this meeting.

2. FDA will grant or deny the Post-CRL Scientific Meeting request within 14 days after receipt of the request.

3. FDA will hold the Post-CRL Scientific Meeting within 90 days after the date the meeting is granted.

4. Applicants are eligible to request a Post-CRL Scientific Meeting even if they have not had a Product Development Meeting.

V. ADDITIONAL PROGRAM ENHANCEMENTS AND ASPIRATIONS

A. Inactive Ingredient Database Enhancement

FDA will update the Inactive Ingredient Database on an ongoing basis, and post quarterly notices of updates made. Such notices will include for each change made during the previous quarter, the new information, and the information that was replaced.

B. Regulatory Science Enhancements

1. FDA will conduct internal and external research to support fulfilment of submission assessment and pre-ANDA commitments set forth in Sections I and III, respectively.

2. Annually, FDA will conduct a public workshop to solicit input from industry and stakeholders for inclusion in an annual list of GDUFA III regulatory science initiatives. Interested parties may propose regulatory science initiatives via email to genericdrugs@fda.hhs.gov. After considering Industry and stakeholder input, FDA will post the list on FDA's website.

3. If Industry forms a GDUFA III regulatory science working group, then upon request of the working group to the Director of the Office of Research and Standards in the Office of Generic Drugs, FDA will meet with the working group twice yearly to discuss current and emerging challenges and concerns. FDA will post minutes of these meetings on its website.

4. Annually, FDA will report on its website the extent to which GDUFA regulatory science-funded projects support the development of generic drug products, the generation of evidence needed to support efficient assessment and timely approval of ANDAs, and the establishment of new approaches to evaluate generic drug equivalence.

C. Other Pre-ANDA and Assessment Meeting Program Aspirations

FDA aspires to continually improve the effectiveness of its Pre-ANDA and ANDA Assessment Meeting activities.

VI. DMF ASSESSMENT PROGRAM ENHANCEMENTS

A. Communication of DMF Assessment Comments

1. FDA will ensure that DMF assessment comments submitted to the DMF holder are issued at least in parallel with the issuance of review comments relating to the DMF for the ANDA.

2. This commitment applies to comments to the applicant issued in any ANDA CRL

and comments issued in the first IR letter by the drug product assessment discipline.

B. Teleconferences to Clarify DMF First Cycle Assessment Deficiencies

1. FDA will grant and conduct teleconferences when requested to clarify deficiencies in first cycle DMF deficiency letters.

2. DMF holders must request such teleconferences in writing within 30 days of issuance of the first cycle DMF deficiency letter, identifying specific issues to be addressed. FDA may initially provide a written response to the request for clarification, but if the DMF holder indicates that a teleconference is still desired, FDA will schedule the teleconference.

3. FDA will strive to grant such teleconferences within 30 days of receipt of the initial teleconference request, giving priority to DMFs based on the priority of the referencing ANDA.

4. In lieu of a teleconference, the DMF holder may submit a request for an email exchange between FDA and the DMF holder. The request must identify specific issues to be addressed. After FDA responds to the request, the DMF holder may submit, and FDA will respond to, one follow-up email to obtain additional clarification.

C. DMF First Adequate Letters

Once a DMF has undergone a full scientific assessment and has no open issues related to the assessment of the referencing ANDA, FDA will issue a First Adequate Letter.

D. DMF No Further Comment Letters

Once a DMF has undergone a full scientific assessment and the ANDA referencing the DMF has been approved or tentatively approved, FDA will issue a ''no further comment'' letter.

E. DMF Review Prior to ANDA Submission

1. A holder of a DMF may submit a request for assessment of the DMF six months prior to the planned submission date for: 1) an original ANDA, 2) an ANDA amendment containing a response to a CRL, or 3) an amendment seeking approval of an ANDA that previously received a tentative approval. In each case, the submission must include reference to a DMF for which FDA has not conducted a substantive assessment, and one of the following criteria must be met:

a. All patents and exclusivities will expire within 12 months of the planned submission date;

b. The submission is for a drug product for which there are not more than three approved drug products listed in FDA's Approved Drug Products With Therapeutic Equivalence Evaluations (the ''Orange Book''), for which there are no blocking patents or exclusivities listed for the RLD, and the ANDA applicant is not seeking approval for less than all of the conditions of use on the RLD labeling, e.g., a ''carve-out.'' In other words, there are fewer than four approved therapeutically equivalent drug products, including the RLD, listed in the Orange Book, no blocking patents or unexpired exclusivities for the RLD in the Orange Book, and the applicant is not seeking to ''carve out'' any conditions of use;

c. The submission is for a drug product that could help mitigate or resolve a drug shortage and prevent future shortages, including submissions related to products that are listed on FDA's Drug Shortage List at the time of the submission;

d. The submission is for a drug product that either could help address a public health emergency declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the PHS Act, or anticipated under the same criteria as apply to such a declaration; or

e. The submission is for a drug product for which (1) there is only one approved drug product listed in the Prescription Drug Product List (i.e., the ''Active Section'') of the Orange Book and that product is approved under an ANDA (i.e., the RLD is in the ''Discontinued Section'' and there is not more than one ANDA in the ''Active Section''); (2) the approved ANDA for the drug product listed in the ''Active Section'' was not approved pursuant to a suitability petition under section 505(j)(2)(C) of the FD&C Act; (3) there are no blocking patents or exclusivities for the RLD; and (4) the submission does not qualify for prioritization under any other factor listed in MAPP 5240.3 Rev. 5: Prioritization of the Review of Original ANDAs, Amendments, and Supplements.

2. A holder of a DMF may submit a request for assessment of the DMF six months prior to the planned submission date for a PAS to add a new API source, provided that:

a. The PAS is for a drug product that could help mitigate or resolve a drug shortage and prevent future shortages, including submissions related to products that are listed on FDA's Drug Shortage List at the time of the submission; or

b. The PAS is for a drug product that either could help address a public health emergency declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the PHS Act, or anticipated under the same criteria as apply to such a declaration.

3. To be eligible for this review, a DMF holder must submit with its request for review:

a. at least one Letter of Authorization with one pre-assigned ANDA number;

b. a reference to the corresponding RLD listed in the Orange Book; and

c. documentation that the DMF holder has paid a GDUFA DMF fee as described in section 744B(a)(2)(A) of the FD&C Act (21 U.S.C. 379j–41(a)(2)(A)) for the current fiscal year.

F. FDA Assessment of Solicited DMF Amendments

1. FDA will assess solicited DMF amendments related to original ANDAs and PASs upon receipt even if the original ANDA or PAS in which the DMF is referenced is not currently under assessment.

2. Such assessments will be conducted based on the assessment status of the DMF and other disciplines in the related ANDAs, with priority being given to those amendments related to ANDAs for which acceptability of the DMF assessment may result in an approval.

G. FDA Communication Related to DMF Amendments and ANDAs

FDA will communicate publicly to industry that prior to submitting a DMF amendment, the DMF holder should coordinate with the ANDA applicant that references the DMF to avoid delaying approval or tentative approval of the ANDA.

VII. FACILITIES

A. Foreign Regulators

1. Export Support and Education of Other Health Authorities: FDA will support the export of safe and effective pharmaceutical products by the U.S.-based pharmaceutical industry, including but not limited to providing timely updates to FDA's Inspection Classification Database as described below, and educating other health authorities regarding FDA's surveillance inspection program and the meaning of inspection classifications.

2. Communications to Foreign Regulators: Upon receipt of a written or email request by an establishment physically located in the U.S. that has been included as part of a marketing application submitted to a foreign regulator, issue within 30 days of the date of receipt of the request a written communication to that foreign regulator conveying the current compliance status for the establishment.

B. Communication Regarding Inspections

1. When FDA conducts a preapproval inspection of a facility or site named in the ANDA, PAS, or associated Type II DMF and identifies outstanding issues that could prevent approval of an ANDA or PAS, the applicant will be notified that issues exist through an IR, DRL or CRL pursuant to Section II(B) above.

2. FDA agrees to communicate to the facility owner final inspection classifications that do not negatively impact approvability of any pending application within 90 days of the end of the inspection.

3. FDA agrees to ongoing periodic engagement with industry stakeholders to provide updates on Agency activities and seek stakeholder feedback.

C. GDUFA III Inspection Classification Database

The Inspection Classification Database will be updated every 30 days and will reflect FDA's final assessment of the facility or site following an FDA inspection and assessment of the inspected entity's timely response to any documented observations. FDA will update the existing publicly available Inspection Classification Database webpage and will develop communication materials to provide further information to industry and foreign regulators on how FDA determines which facilities to select for a drug surveillance inspection, including how FDA uses its risk-based site selection model to determine the frequency of surveillance inspections.

D. Post-Warning Letter Meetings

1. An eligible facility described in section VII(D)(3) may request a meeting with FDA regarding the facility's remediation for deviations identified in a warning letter (Post-Warning Letter Meeting).

a. This meeting generally will take place 6 months or later after the facility submits an initial response to an FDA warning letter.

b. A facility may request that the meeting take place prior to 6 months after an initial response to a warning letter has been submitted. However, it is at FDA's discretion to grant an earlier meeting if the Agency determines it would be beneficial to both parties.

2. The purpose of the Post-Warning Letter Meeting is to obtain preliminary feedback from FDA on the adequacy and completeness of the facility's corrective action plans.

3. To be eligible for the Post-Warning Letter Meeting:

a. The facility Current Good Manufacturing Practice (CGMP) compliance status is ''Official Action Indicated'' as a result of an FDA inspection;

b. The facility has paid a GDUFA facility fee as described in section 744B(a)(4) of the FD&C Act for the current fiscal year, or is named in a pending ANDA application; and

c. The regulatory action (e.g., warning letter) is limited only to violations or deviations from Section 501 of the FD&C Act (21 U.S.C. 351) related to human drug manufacturing, including manufacturing of a drug-device combination product.

4. The meeting request will be granted only if the facility has submitted to FDA a thorough and complete corrective action and preventive action (CAPA) plan that addresses all items cited in the warning letter, and reasonable progress has been made toward remediation.

5. Any supplemental information submitted by a facility on remediation progress to be discussed at the meeting must be submitted at least 60 days prior to the meeting.

6. FDA may deny a request for a Post-Warning Letter Meeting if FDA determines that a facility is ineligible for a meeting or does not appear to be ready for a meeting as evidenced by an incomplete CAPA plan, and/or insufficient progress being made to remediate the facility issues. If FDA denies the meeting:

a. In general, FDA intends to respond briefly with comments regarding why the meeting package is not sufficiently developed or complete (e.g., where the facility has not presented a proposed CAPA plan for all items in the warning letter or where the firm does not appear to have made reasonable efforts to implement its proposed CAPA plan).

b. A facility may resubmit a new meeting request no sooner than 3 months after the first meeting request is denied by FDA.

7. Only two Post-Warning Letter Meeting requests per warning letter may be made under this section.

8. FDA may defer a Post-Warning Letter Meeting if FDA has made a decision that a reinspection is the most appropriate next step (i.e., defer in favor of re-inspection). In this case, FDA will notify the facility of the decision to re-inspect rather than grant a meeting.

9. FDA may schedule meetings by video conference, teleconference, or face-to-face, at FDA's discretion.

10. The following goals apply to FDA's decision to grant, deny, or defer in favor of reinspection a Post-Warning Letter Meeting:

a. In FY 2024, 50 percent of eligible requests within 30 days of request.

b. In FY 2025, 70 percent of eligible requests within 30 days of request.

c. In FY 2026 and FY 2027, 80 percent of eligible requests within 30 days of request.

11. The commitment to hold a Post-Warning Letter Meeting:

a. Does not preclude FDA from taking any regulatory actions necessary, including a follow-up inspection at any time (including prior to the Post-Warning Letter Meeting); and

b. As with other regulatory meetings, FDA advice is not binding on the Agency.

12. Guidance related to Post-Warning Letter Meeting process set forth in this section VII(D):

a. FDA will issue guidance regarding the Post-Warning Letter Meeting process, including recommendations on items facilities should submit as part of a meeting request.

b. If more than 50 percent of first-time meeting requests are denied because FDA makes an assessment that the facility is not ready, FDA agrees to take appropriate action to provide additional information on meeting requests, which could include updating the guidance described in VII(D)(12)(a) to provide further information on how facilities can avoid issues that have commonly led to meeting requests being denied.

E. Generic Drug Manufacturing Facility Re-inspection

1. An eligible facility as described in section VII(E)(2) may request a re-inspection.

2. To be eligible for the facility re-inspection process reflected in this section:

a. The facility CGMP compliance status is ''Official Action Indicated'' as a result of an FDA inspection;

b. The facility has paid a GDUFA facility fee as described in section 744B(a)(4) of the FD&C Act for the current fiscal year, or is named in a pending ANDA application; and

c. The regulatory action (e.g., warning letter) is limited only to violations or deviations from Section 501 of the FD&C Act related to human drug manufacturing, including manufacturing of a drug-device combination product.

3. FDA will review the request and if FDA determines that the requesting facility has appropriately completed CAPAs that sufficiently address all of the deficiencies in a warning letter, with the exception of ongoing monitoring, and FDA agrees that the facility appears ready for inspection, FDA will generate an inspectional assignment.

4. FDA agrees to notify the facility of the Agency's decision to re-inspect within 30 days of receipt of the request for re-inspection.

5. If FDA declines the request to reinspect:

a. FDA agrees to notify the facility of its decision and provide a brief high-level explanation, for example, that the firm has not made sufficient progress to complete certain CAPAs identified as necessary to resolve a violation cited in the warning letter.

b. The facility may submit a second request for a re-inspection no earlier than 3 months after receiving FDA's initial decision.

c. If the second request is denied, facility will be considered to no longer meet the eligibility criteria in section VII(E)(2).

6. The processes and timelines set forth in this section apply only to the first reinspection after a warning letter. If the warning letter is not resolved after reinspection, the facility will be considered to no longer meet the eligibility criteria in section VII(E)(2).

7. If a re-inspection request is granted, FDA agrees to notify the facility and issue an inspectional assignment in conjunction with the notification. The applicable goals for domestic facilities are:

a. In FY 2024, for 60 percent of the requests for reinspection that are granted, FDA will re-inspect the facility within 4 months of the letter to the facility indicating FDA's intent to reinspect.

b. In FY 2025, for 70 percent of the requests for reinspection that are granted, FDA will re-inspect the facility within 4 months of the letter to the facility indicating FDA's intent to reinspect.

c. In FY 2026 and FY 2027, for 80 percent of the requests for reinspection that are granted, FDA will re-inspect the facility within 4 months of the letter to the facility indicating FDA's intent to reinspect.

8. The applicable goals for international facilities are:

a. In FY 2024, for 60 percent of the requests for reinspection that are granted, FDA will re-inspect the facility within 8 months of the letter to the facility indicating FDA's intent to re-inspect.

b. In FY 2025, for 70 percent of requests for reinspection that are granted, FDA will re-inspect the facility within 8 months of the letter to the facility indicating FDA's intent to re-inspect.

c. In FY 2026 and FY 2027, for 80 percent of requests for reinspection that are granted, FDA will re-inspect the facility within 8 months of the letter to the facility indicating FDA's intent to re-inspect.

VIII. CONTINUED ENHANCEMENT OF USER FEE RESOURCE MANAGEMENT

A. Sustainability of GDUFA Program Resources

1. FDA is committed to ensuring the sustainability of the GDUFA program resources and to enhancing the operational agility of the GDUFA program.

2. FDA will build on the financial enhancements included in GDUFA II and continue activities in GDUFA III to ensure optimal use of user fee resources and the alignment of staff to workload through the continued maturation and assessment of the Agency's resource capacity planning capability.

3. FDA also will continue activities to promote transparency of the use of financial resources in support of the GDUFA program.

B. Resource Capacity Planning

1. FDA will continue activities to mature the Agency's resource capacity planning function, including utilization of modernized time reporting to support enhanced management of GDUFA resources in GDUFA III and implementation of the Capacity Planning Adjustment (CPA).

2. Resource Capacity Planning Implementation

a. By the end of the second quarter of FY 2023, FDA will publish an implementation plan that will describe how resource capacity planning and time reporting will continue to be utilized during GDUFA III. This implementation plan will address topics relevant to the maturation of resource capacity planning including, but not limited to, detailing FDA's approach to:

i. The continued maturation of the Agency's resource capacity planning capability;

ii. The continual improvement of time reporting and its utilization in the CPA;

iii. The integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes; and

iv. The implementation of the CPA, with a first year of adjustment for FY 2024 user fees.

b. FDA will provide annual updates on the FDA website on the Agency's progress relative to activities detailed in this implementation plan by the end of the second quarter of each subsequent fiscal year.

c. FDA will document in the annual GDUFA Financial Report how any CPA fee revenues are being utilized.

d. Resources obtained from the CPA shall be used, consistent with user fee appropriations, to support CDER or ORA staff engaged in GDUFA program work, or other non-CDER staff who are directly supporting GDUFA review work.

e. The CPA shall be limited to workload driven by:

i. ANDA Originals and Resubmissions/Amendments

ii. ANDA Supplements (PAS and ''Changes Being Effected'' (CBE) supplements) and Amendments

iii. Controlled Correspondence as defined in Section XI(I)–(J)

iv. Pre-ANDA Meetings, which include Pre-Submission, Product Development, and Pre-Submission PSG Meetings

v. Surveillance inspections

vi. Post-marketing safety activities

vii. Suitability Petitions

C. Resource Capacity Planning Assessment

1. By the end of FY 2025, an independent contractor will complete and publish an evaluation of the resource capacity planning capability. This will include an assessment of the following topics:

a. The ability of the CPA to forecast resource needs for the GDUFA program, including an assessment of the scope of the workload drivers in the CPA and their ability to represent the overall workload of the GDUFA program;

b. Opportunities for the enhancement of time reporting toward informing resource needs; and

c. The integration and utilization of resource capacity planning information within resource and operational decision-making processes of the GDUFA program.

2. The contractor will provide options and recommendations in the evaluation regarding the continued enhancement of the above topics as warranted. The evaluation findings and any related recommendations will be discussed at the FY 2026 GDUFA 5–year financial plan public meeting. The findings and recommendations of the evaluation may inform the CPA methodology for future reauthorizations.

D. Financial Transparency and Efficiency

1. FDA is committed to ensuring GDUFA user fee resources are administered, allocated, and reported in an efficient and transparent manner. FDA will conduct activities

to evaluate the financial administration of the GDUFA program to help identify areas to enhance operational and fiscal efficiency. FDA will also conduct activities to enhance transparency of how GDUFA program resources are used.

2. FDA will publish a GDUFA 5–year financial plan no later than the second quarter of FY 2023. FDA will publish updates to the 5–year plan no later than the second quarter of each subsequent fiscal year.

3. FDA will convene a public meeting no later than the third quarter of each fiscal year starting in FY 2024 to discuss the GDUFA 5–year financial plan, along with the Agency's progress in implementing modernized time reporting and resource management planning.

E. Improving the Hiring of Review Staff

1. Enhancements to the generic drug review program require that FDA hire the necessary technical and scientific experts to efficiently conduct assessments of generic drug applications and supporting activities.

2. During GDUFA III, FDA will:

a. Hire 128 staff for the generic drug review program in FY 2023; and

b. Confirm progress in the hiring of GDUFA III staff in the GDUFA 5–year financial plan.

IX. GUIDANCE AND MAPPS

A. FDA will draft or modify relevant Manuals of Policies and Procedures (MAPPs) to reflect the commitments and goals in this Commitment Letter, including, but not limited to, the following:

1. To direct project managers, assessors, and other assessment program staff to actively work towards an action for an ANDA with a missed or extended goal date.

2. To revise MAPP 5200.12 Communicating Abbreviated New Drug Application Review Status Updates with Industry, to include communications related to imminent actions on or before April 30, 2023.

B. FDA will issue a Federal Register Notice on or before April 30, 2023, to solicit public comment on the content of Appendix A in the guidance for industry on ANDA Submissions—Amendments to Abbreviated New Drug Applications Under GDUFA (July 2018) and will use evaluations and/or training to assure consistency in ANDA amendment classification.

C. FDA will issue a MAPP on the process for Reclassification of Facility-Based Major CRL Amendments set forth in section II(C)(7) on or before June 30, 2024.

D. FDA will issue a MAPP on the prioritization of FDA assessment of solicited DMF amendments described in section VI(F)(2) on or before June 30, 2024.

E. FDA will issue guidance clarifying the regulatory status of active pharmaceutical ingredient-excipient mixtures for GDUFA purposes.

X. PERFORMANCE REPORTING

A. Monthly Reporting Metrics: FDA will publish the following monthly metrics on its website, using a consistent, publicly disclosed reporting methodology:

Number of ANDAs and amendments, CBE supplements, and PASs submitted in the reporting month delineated by type of submission:

2. Number of ANDAs and PASs FDA refused for receipt in the reporting month:

3. Number of actions taken in the reporting month delineated by the type of action. For purposes of the metrics, actions shall include final approvals, tentative approvals, CRLs, IRs, and DRLs (or other such nomenclature as FDA determines to reflect the concepts of an information request or CRL):

4. Number of finalized DMF Completeness Assessments in the reporting month;

5. Number of DMF fees paid in the reporting month; and

6. Number of first-cycle approvals and tentative approvals in the reporting month.

B. Quarterly Reporting Metrics: FDA will publish the following quarterly metrics on its website, using a consistent, publicly disclosed reporting methodology:

1. Number of ANDAs and PASs withdrawn in each reporting month;

2. Number of ANDAs awaiting applicant action;

3. Number of ANDAs awaiting FDA action;

4. Mean and median approval and tentative approval times for the quarterly action cohort,

5. Number of original ANDAs for Complex Generic Products submitted;

6. Number of requests for reclassification of a Facility-Based Major CRL Amendment received, and number of requests granted and denied; and

7. Number of Level 1 and Level 2 Controlled Correspondence submitted.

C. Fiscal Year Performance Report Metrics: FDA will publish the following metrics annually as part of the GDUFA Performance Report:

1. Mean and median approval and tentative approval times for ANDAs by FY receipt cohort;

2. Mean and median ANDA approval times, including separate reporting of mean and median times for first-cycle approvals FY receipt cohort;

3. Mean and median number of ANDA assessment cycles to approval and tentative approval by FY receipt cohort;

4. Number of applications received and refused to receive, and average time to receipt decision;

5. Number of GDUFA-related meetings and teleconferences requested, granted, denied, and conducted, broken down by type of meeting or teleconference, and in addition for Post-Warning Letter Meetings, the number deferred in favor of re-inspection;

6. Number of inspections conducted by domestic or foreign establishment location and inspection type (preapproval inspection, surveillance, bioequivalence clinical and bioequivalence analytical) and facility type (finished dosage form, API);

7. Median time from beginning of inspection to Form FDA 483 issuance;

8. Median time from Form FDA 483 issuance to Warning Letter, Import Alert and Regulatory Meeting for inspections with final classification of ''Official Action Indicated'' (or equivalent),

9. Median time from date of Warning Letter, Import Alert or Regulatory Meeting to resolution of the ''Official Action Indicated'' status (or equivalent);

10. Number of ANDAs accepted for standard assessment and priority assessment;

11. Percentage of suitability petitions completed within 6 months after FDA completes the completeness assessment, the total number submitted, and total number completed;

12. Number of citizen petitions to determine whether a listed drug has been voluntarily withdrawn from sale for reasons of safety or effectiveness pending a substantive response for more than 270 days from the date of receipt;

13. Percentage of ANDA proprietary name requests evaluated within 180 days of receipt;

14. Number of DMF First Adequate Letters issued;

15. Number of teleconferences granted, and number of email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in first cycle DMF deficiency letters;

16. Percent of PSGs for non-Complex Product NCE NDAs within two years of NDA approval;

17. Percent of PSGs for Complex Product NDAs, including NCEs, published within two and three years of NDA approval;

18. Percentage of facility re-inspections carried out within 4 or 8 months after the letter to the facility indicating FDA's intent to reinspect for domestic or foreign facilities, respectively;

19. For the total number of original ANDAs, amendments, PASs, PAS amendments, and meeting requests submitted in a fiscal year, FDA will publish the number of actions completed (as of the annual publication date), and the percent completed by the goal date. FDA also will publish this data annually on its website, further enumerated by goal-date subcategory, and will include metrics regarding timeframes for acting on meeting requests;

a. For example, in the GDUFA Performance Report, the priority PAS submission goal will be reported as the number of actions and the percent completed combined for the 4-, 8- and 10-month goals

b. For the Annual Web Posting, the priority PAS submission goals will be reported as the number of actions and the percent completed individually for the 4-, 8- and 10-month goals; and

20. Percent Controlled Correspondence Level 1 and Level 2 responded to within the applicable goal date (i.e., 60 and 120 days, respectively);

21. Number of missed goal dates for original ANDAs by more than 6, 9, and 12 months.

D. Fiscal Year Web Posting

In addition to the data that will be reported annually on the web described in section XI(C)(19), FDA will also post the following data annually on its website:

1. The number of requests for review of a DMF prior to ANDA or PAS submission, as describe in sections VI(E)(1) and VI(E)(2), the number granted, and the number completed;

2. Number of priority and non-priority ''off-cycle'' solicited DMF amendments reviewed as described in section VI(F); and

3. Number of original approvals taken that are Imminent Actions.

XI. DEFINITIONS

A. Act on—with respect to an application, means FDA will either issue a CRL, an approval, a tentative approval, or a refuse-to-receive action.

B. Ambiguity in the Controlled Correspondence response—means the Controlled Correspondence response or a critical portion of it merits further clarification.

C. Review Status Update—means a response from the RPM to the applicant to update the applicant concerning, at a minimum, the categorical status of relevant assessment disciplines with respect to the submission at that time. The RPM will advise the applicant that the update is preliminary only, based on the RPM's interpretation of the submission, and subject to change at any time.

D. Capacity Planning Adjustment—Methodology that annually adjusts inflation-adjusted target revenue to account for additional resource needs due to sustained increases in workload for the GDUFA program.

E. Complete Response Letter—refers to a written communication to an applicant or DMF holder from FDA usually describing all of the deficiencies that the Agency has identified in an ANDA (including pending amendments) or a DMF that must be satisfactorily addressed before the ANDA can be approved. Complete response letters will reflect a Complete Assessment, which includes an application-related facilities assessment and will require a complete response from industry to restart the clock. Refer to 21 CFR 314.110 for additional details. When a citizen petition may impact the approvability of the ANDA,

FDA will strive to address, where possible, valid issues raised in a relevant citizen petition in the complete response letter. If a citizen petition raises an issue that would delay only part of a complete response, a response that addresses all other issues will be considered a complete response.

F. Complete Assessment—refers to a full division-level assessment from all relevant assessment disciplines, including inspections, and includes other matters relating to the ANDAs and associated DMFs as well as consults with other Agency components.

G. Complex Product—generally includes:

1. Products with complex active ingredients (e.g., peptides, polymeric compounds, complex mixtures of APIs, naturally sourced ingredients); complex formulations (e.g., liposomes, colloids); complex routes of delivery (e.g., locally acting drugs such as dermatological products, complex ophthalmological products, and otic dosage forms that are formulated as suspensions, emulsions or gels) or complex dosage forms (e.g., transdermal systems, metered dose inhalers, extended release injectables)

2. Complex drug-device combination products (e.g., pre-filled auto-injector products, metered dose inhalers); and

3. Other products where complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement.

H. Complex Generic Product—refers to a generic version of a Complex Product.

I. Controlled Correspondence—Level 1—means correspondence submitted to the Agency, by or on behalf of a generic drug manufacturer or related industry:

1. Requesting information on a specific element of generic drug product development:

a. Prior to ANDA submission;

b. After a PSG Teleconference if a prospective applicant or applicant seeks further feedback from FDA;

c. After issuance of a CRL or tentative approval;

d. After ANDA approval; or

2. Concerning post-approval submission requirements that are not covered by CDER post-approval changes guidance and are not specific to an ANDA.

J. Controlled Correspondence—Level 2—means correspondence that meets the definition of Level 1 correspondence, and:

1. Involves evaluation of clinical content;

2. Requests a Covered Product Authorization and review of bioequivalence protocols for development and testing that involves human clinical trials for an ANDA where the RLD is subject to a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU);

3. Requests a Covered Product Authorization to obtain sufficient quantities of an individual covered product subject to a REMS with ETASU when development and testing does not involve clinical trials;

4. Requests evaluations of alternative bioequivalence approaches (e.g., pharmacokinetic, in vitro, clinical); or

5. Requires input from another office or center, e.g., questions regarding device constituent parts of a combination product.

K. Covered Product Authorization—a letter from FDA authorizing an eligible product developer to obtain sufficient quantities of an individual covered product subject to a REMS with ETASU for product development and testing purposes, as described in section 610 of Division N of the Further Consolidated Appropriations Act, 2020 (21 U.S.C. 355–2), commonly referred to as the ''CREATES Act.''

L. Days—unless otherwise specified, means calendar days.

M. Discipline Review Letter—means a letter used to convey preliminary thoughts on possible deficiencies found by a discipline assessor and/or assessment team for its portion of the pending application at the conclusion of the discipline assessment.

N. Earliest lawful ANDA approval date—the first date on which no patent or exclusivity prevents approval of an ANDA.

O. First Adequate Letter—a communication from FDA to DMF holder indicating that the DMF has no open issues related to the assessment of the referencing ANDA. This communication is issued only at the conclusion of the first DMF assessment cycle that determines the DMF does not have any open issues.

P. First Generic—any received ANDA: (1) for a First Applicant as described in section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act or for which there are no blocking patents or exclusivities; and (2) for which there is no previously approved ANDA for the drug product.

Q. Information Request—means a communication that is sent to an applicant during an assessment to request further information or clarification that is needed or would be helpful to allow completion of the discipline assessment.

R. Major Amendment—means a Major Amendment as described in the guidance for industry on ANDA Submissions Amendments to Abbreviated New Drug Applications Under GDUFA (July 2018), and any subsequent revision.

S. Mid-point of assessment cycle The midpoint of an assessment cycle is half the length of an assessment period plus or minus 30 days.

T. Minor Amendment—means a minor amendment as described in the guidance for industry on ANDA Submissions Amendments to Abbreviated New Drug Applications Under GDUFA (July 2018), and any subsequent revision.

U. Priority—means submissions affirmatively identified as eligible for expedited assessment pursuant to MAPP 5240.3, Prioritization of the Review of Original ANDAs, Amendments and Supplements, as revised (the CDER Prioritization MAPP).

V. Significant Major deficiency—means a major deficiency, the resolution of which is required before the continued assessment by multiple disciplines, e.g., a reformulation, or a major deficiency that impacts the test drug product used in a bioequivalence study.

W. Small Issue—for the purposes of Imminent Actions in section II(B)(3), means a deficiency that can be assessed by FDA within 60 days because it can be addressed by: 1)a clarification of scientific information regarding data already submitted, 2) the limited submission of additional data, or 3) the submission of administrative information (e.g., completion of a form or a change in an address).

X. Standard—means submissions not affirmatively identified as eligible for expedited assessment pursuant to the CDER Prioritization MAPP.

Y. Teleconference—means a verbal communication by telephone, and not a written response, unless otherwise agreed to by the applicant.

Z. Unsolicited Amendment—an amendment with information not requested by FDA except for those unsolicited amendments considered routine or administrative in nature that do not require scientific review (e.g., requests for final ANDA approval, patent amendments, and general correspondence).

APPENDIX: PRIORITIZATION OF SUITABILITY PETITIONS

Prior to GDUFA III, FDA received approximately 20–30 suitability petitions per year and had approximately 170 suitability petitions currently pending as of July 2021. Pursuant to this Commitment Letter, in GDUFA III FDA has agreed to set goal dates for review and response to suitability petitions. To receive a goal date, pending petitions submitted prior to FY 2024 must be withdrawn and resubmitted.

If FDA does not respond to all petitions submitted in a given fiscal year, FDA has committed to prioritizing suitability petitions that are carried over to the following fiscal year over new petitions received in that fiscal year (subject to the prioritization outlined in section III(B)(6)). The following hypothetical example describes how FDA will prioritize suitability petitions if FDA is unable to respond to all suitability petitions in a given fiscal year. This example assumes a significantly higher number of incoming petitions and a high number of carryover petitions to illustrate how petitions that are carried over will be prioritized.

Example

For FY 2024, FDA's goal is to respond to 50 percent of all suitability petitions received within six months of the completeness assessment, up to a maximum of 50 suitability petitions. In FY 2024, FDA receives and performs the completeness assessment for 100 suitability petitions. To meet the goal, FDA must respond to 50 of those petitions within six months after the completeness assessment. At the end of FY 2024, FDA has responded to 50 petitions within 6 months, and 10 in greater than six months. FDA therefore met the FY 2024 goal of 50 percent within six months (i.e., 50 petitions), and the additional 40 petitions still pending roll into FY 2025.

For FY 2025, FDA's goal is to respond to 70 percent of all suitability petitions received within six months of the completeness assessment, up to a maximum of 70 suitability petitions. In FY 2025, FDA receives 40 suitability petitions. To meet the FY 2025 goal, FDA must respond to 28 of those petitions within six months of the completeness assessment. FDA will prioritize any suitability petitions received in FY 2025 prioritized as outlined in section III(B)(6) and the 40 pending petitions from FY 2024 over any other suitability petitions received in FY25, in that order. By the end of FY 2025, FDA has responded to all 40 petitions from the FY 2024 cohort and 28 of the 40 from FY 2025 within 6 months of the completeness assessment. Twelve petitions from the FY 2025 cohort remain pending. FDA has met the FY 2025 goal, and the remaining 12 petitions still pending will be carried over into FY 2026 and prioritized.

BIOSIMILAR BIOLOGICAL PRODUCT REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027

I. ENSURING THE EFFECTIVENESS OF THE BIOSIMILAR BIOLOGICAL PRODUCT REVIEW PROGRAM

A. Review Performance Goals

B. Program for Enhanced Review Transparency and Communication for Original 351(k) BLAs

C. Guidance

D. Review of Proprietary Names to Reduce Medication Errors

E. Major Dispute Resolution

F. Clinical Holds

G. Special Protocol Question Assessment and Agreement

H. Meeting Management Goals

II. ENHANCING BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCT DEVELOPMENT AND REGULATORY SCIENCE

A. Promoting Best Practices in Communication between FDA and Sponsors During Application Review

B. Inspections and Alternate Tools to Evaluate Facilities

BIOSIMILAR BIOLOGICAL PRODUCT AUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FOR FISCAL YEARS 2023 THROUGH 2027

This document contains the performance goals and procedures for the Biosimilar User Fee Act (BsUFA) reauthorization for fiscal years (FYs) 2023–2027, known as BsUFA III. 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 biosimilar biological product review program that are important for facilitating timely access to safe and effective biosimilar medicines for patients. FDA is committed to meeting the performance goals specified in this letter, enhancing management of BsUFA resources, and ensuring BsUFA user fee resources are administered, allocated, and reported in an efficient and transparent manner.

Under BsUFA III, FDA is committed to ensuring effective scientific coordination and review consistency, as well as efficient governance and operations across the biosimilar biological product review program.

FDA and the regulated industry will periodically and regularly assess the progress of the biosimilar biological product review program throughout BsUFA III. 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 biosimilar biological product review program.

I. ENSURING THE EFFECTIVENESS OF THE BIOSIMILAR BIOLOGICAL PRODUCT REVIEW PROGRAM

A. REVIEW PERFORMANCE GOALS

1. Original and Resubmitted Biosimilar Biological Product Applications

a. Review and act on 90 percent of original biosimilar biological product application submissions within 10 months of the 60 day filing date.

b. Review and act on 90 percent of resubmitted original biosimilar biological product applications within 6 months of receipt.

2. Original and Resubmitted Supplemental Biosimilar Biological Product Applications

a. Review and act on the following supplements within 3 months of receipt:

i. Category A: Supplements seeking to update the labeling for a licensed biosimilar or interchangeable product with regards to safety information that has been updated in the reference product labeling and is applicable to one or more indications for which the biosimilar or interchangeable product is licensed.

b. Review and act on the following supplements within 4 months of receipt:

i. Category B: Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product when the submission does not include new data sets (other than analytical in vitro data obtained by use of physical, chemical and/or biological function assays, if needed to support the scientific justification for extrapolation), provided that:

1) The supplement does not seek a new route of administration, dosage form, dosage strength, formulation or presentation; and

2) If the supplement is subject to section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the supplement contains an up-to-date agreed initial pediatric study plan (iPSP).

ii. Category C: Supplements seeking to remove an approved indication for a licensed biosimilar or interchangeable product.

c. Review and act on the following supplements within 6 months of receipt:

i. Category D: Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product when the submission:

1) Contains new data sets (other than efficacy data, data to support a supplement seeking an initial determination of interchangeability, or only analytical in vitro data obtained by use of physical, chemical and/or biological function assays); or

2) Does not contain new data sets (other than analytical in vitro data obtained by use of physical, chemical and/or biological function assays) but is subject to section 505B(a) of the FD&C Act, and the supplement does not contain an up-to-date agreed iPSP.

d. Review and act on the following supplements within 10 months of receipt for the original submissions, and within 6 months of receipt for resubmissions:

i. Category E: Supplements seeking licensure for an additional indication for a licensed biosimilar or interchangeable product and containing efficacy data sets.

ii. Category F: Supplements seeking an initial determination of interchangeability.

e. FDA will issue a letter to the applicant for 90% of original Category A through D supplements within 60 calendar days of receipt. The letter will acknowledge receipt of the submission and provide the date for FDA to take action on the supplement.

i. Applicants may include in their cover letter a request that FDA not approve the supplement before a certain date, as long as that date is not later than the BsUFA goal date.

f. A filing letter will be issued to the applicant for 90% of original Category E and F supplements within 74 calendar days of receipt. Consistent with the underlying principles articulated in the Good Review Management Principles and Practices (GRMP) guidance, the letter will acknowledge receipt of the submission and inform the applicant of the planned review timeline and whether substantive review issues were identified. If no substantive review issues were identified during the filing review, FDA will so notify the applicant.

3. Original Manufacturing Supplements

a. Review and act on 90 percent of manufacturing supplements requiring prior approval within 4 months of receipt.

b. Review and act on 90 percent of all other manufacturing supplements within 6 months of receipt.

4. Goals Summary Tables

TABLE 1—ORIGINAL AND RESUBMITTED APPLICATIONS AND CATEGORY A–F SUPPLEMENTS

Original Biosimilar Biological Product Application Submissions	90% in 10 months of the 60 day filing date
Resubmitted Original Biosimilar Biological Product Applications	90% in 6 months of the receipt date
Category A Supplements. (original and resubmitted).	• FY 2023: 70% in 3 months of the receipt date • FY 2024: 80% in 3 months of the receipt date • FY 2025: 90% in 3 months of the receipt date • FY 2026: 90% in 3 months of the receipt date • FY 2027: 90% in 3 months of the receipt date
Category B and C Supplements. (original and resubmitted).	• FY 2023: 70% in 4 months of the receipt date • FY 2024: 80% in 4 months of the receipt date • FY 2025: 90% in 4 months of the receipt date • FY 2026: 90% in 4 months of the receipt date • FY 2027: 90% in 4 months of the receipt date
Category D Supplements. (original and resubmitted).	• FY 2023: 70% in 6 months of the receipt date • FY 2024: 80% in 6 months of the receipt date • FY 2025: 90% in 6 months of the receipt date • FY 2026: 90% in 6 months of the receipt date • FY 2027: 90% in 6 months of the receipt date
Original Category E and F Supplements	90% in 10 months of the receipt date
Resubmitted Category E and F Supplements	90% in 6 months of the receipt date

TABLE 2—MANUFACTURING SUPPLEMENTS

	Prior approval	All other
Manufacturing Supplements.	90% in 4 months of the receipt date.	90% in 6 months of the receipt date

5. Review Performance Goal Extensions

a. Major Amendments

i. A major amendment to an original application, supplement with clinical data, 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 study report; major re-analysis of previously submitted study(ies); submission of a risk evaluation and mitigation strategy (REMS) with elements 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 Good Review Management Principles and Practices (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 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 supplement with clinical data, 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.

B. PROGRAM FOR ENHANCED REVIEW TRANSPARENCY AND COMMUNICATION FOR ORIGINAL 351(K) 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 original Biologics License Applications (BLAs) submitted under section 351(k) of the Public Health Service Act (''351(k) BLAs''), including applications that are resubmitted following a Refuse-to-File decision, received from October 1, 2022, through September 30, 2027. 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 biosimilar and interchangeable biological products.

The standard approach for the review of original 351(k) 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 original 351(k) BLA. The Formal Communication Plan may include elements of the standard approach (e.g., a midcycle 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 sponsor 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 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 this 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 BPD Type 4 (pre–351(k) BLA) meeting. This meeting will be attended by the FDA review team, including appropriate senior FDA staff.

a. The BPD Type 4 (pre–351(k) 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 regarding the approach to developing the content for REMS, where applicable, patient labeling (e.g., Medication Guide and Instructions For Use) and, where applicable, the development of a Formal Communication Plan. These discussions will be summarized at the conclusion of the meeting and reflected in the FDA meeting minutes.

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; stability updates, the final audited report of a preclinical study (e.g., toxicology) where the final draft report is submitted with the original application, or a limited amount of the data from an assessment of a single transition from the reference product to the proposed biosimilar biological product, where applicable.

ii. Major components of the application (e.g., the complete analytical similarity assessment, the complete study report of a comparative clinical study or the full study report of necessary immunogenicity 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 BPD Type 4 (pre-351(k) BLA) meeting, at the time of original submission of the application. If the applicant does not have a BPD Type 4 (pre–351(k) 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.A.1.a.

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 goal described in Section I.A.1.b 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 substantive review issues identified during the initial filing review to the applicant in the ''Day 74 letter.'' If no

substantive review issues were identified during the filing review, FDA will so notify the applicant. FDA's filing review represents a preliminary review of the application and is not indicative of deficiencies that may be identified later in the review cycle.

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 timeline for review of the application included in the Day 74 letter for applications in the Program will include:

a. the planned date for the internal mid-cycle review meeting,

b. preliminary plans on whether to hold an Advisory Committee (AC) meeting to discuss the application,

c. a target date for communication of feedback from the review division to the applicant regarding proposed labeling and any postmarket requirements or postmarket commitments the Agency will be requesting.

4. Review performance goals: For original 351(k) BLA submissions that are filed by FDA under the Program, the BsUFA review clock will begin at the conclusion of the 60 calendar 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 original 351(k) BLA submissions within 10 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.

The update should include any significant issues identified by the review team to date, any information requests, and information regarding major concerns with the following:

a. The analytical similarity data, including the potential relevance of any issues (e.g. data analysis issues or potential clinical impact of observed analytical differences), intended to support a demonstration that the proposed biosimilar biological product is highly similar to the reference product.

b. The data intended to support a demonstration of no clinically meaningful differences, including discussion of any immunogenicity issues.

c. The data intended to support a demonstration of interchangeability.

d. CMC issues.

In addition, the update should include preliminary review team thinking regarding the content of the proposed REMS, where applicable, proposed date(s) for the late-cycle meeting, updates regarding plans for the AC meeting (if an AC meeting is anticipated), and other projected milestone dates for the remainder of the review cycle.

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 Advisory Committee (AC) meeting, the following parameters apply:

i. FDA intends to convene AC meetings no later than 2 months prior to the BsUFA 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 sponsor 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 committee 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 prior to the BsUFA 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 before the late-cycle meeting. The package will consist of any discipline review (DR) letters issues to date, 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 content of proposed REMS or other risk management actions, where applicable.

e. Late-Cycle Meeting Discussion Topics: Potential topics for discussion at the late-cycle meeting include:

i. major deficiencies identified to date;

ii. analytical similarity data, including the potential relevance of any issues (e.g. data analysis issues or potential clinical impact of observed analytical differences), intended to support a demonstration that the proposed biosimilar biological product is highly similar to the reference product;

iii. data intended to support a demonstration of no clinically meaningful differences, including discussion of any immunogenicity issues;

iv. data intended to support a demonstration of interchangeability;

v. CMC issues;

vi. inspectional findings identified to date;

vii. issues to be discussed at the AC meeting (if planned);

viii. current assessment of the content of proposed REMS or other risk management actions, where applicable;

ix. information requests from the review team to the applicant; and additional data or analyses the applicant may wish to submit.

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 BsUFA goal date.

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

C. GUIDANCE

FDA and industry share a commitment to ensuring an efficient and effective review process for all applications subject to the BsUFA program.

In light of the new, expedited timelines for supplements, FDA will issue guidance and/or a MAPP on classifying supplements to a licensed 351(k) BLA for purposes of determining review timelines. FDA will publish a draft guidance for public comment and/or a MAPP no later than the end of FY 2023. FDA will work toward the goal of publishing a revised draft or final guidance within 18 months after the close of the public comment period.

D. 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 following performance goals apply to FDA's review of biosimilar biological product proprietary names during the biosimilar biological product development (BPD) phase and during FDA's review of a marketing application:

1. Proprietary Name Review Performance Goals During The BPD Phase

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

b. In 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 biosimilar biological product proprietary name submissions filed within 90 days of receipt. Notify sponsor of tentative acceptance/nonacceptance.

b. A supplemental review will be done meeting the above review performance goals if the proprietary name has been submitted previously (during the BPD phase) and has received tentative acceptance.

c. 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).

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.

E. MAJOR DISPUTE RESOLUTION

1. Procedure: For procedural or scientific matters involving the review of biosimilar biological product applications and supplements (as defined in BsUFA) 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 responses 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).

e. In these cases, once the required information is received by the Agency (including any advice from an advisory committee), the person to whom the appeal was made, again has 30 calendar days from the receipt of the required information in which to either deny or grant 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. Note: If the Agency decides to present the issue to an advisory committee and there are not 30 days before the next scheduled advisory committee, the issue will be presented at the following scheduled committee meeting to allow conformance with advisory committee administrative procedures.

F. 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.

G. 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 related 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., are the clinical endpoints adequate to assess whether there are clinically meaningful differences between the proposed biosimilar biological product and the reference product).

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 any necessary clinical study or studies to prove biosimilarity and/or interchangeability (e.g., protocols for pharmacokinetics and pharmacodynamics studies, protocols for comparative clinical studies that will form the primary basis for demonstrating that there are no clinically meaningful differences between the proposed biosimilar biological product and the reference product, and protocols for clinical studies intended to support a demonstration of interchangeability). For such protocols to qualify for this comprehensive protocol assessment, the sponsor must have had a BPD Type 2b or 3 Meeting, as defined in section I.I, below, 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. 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 protocols assessments and agreement requests completed and returned to sponsor within 45 days.

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

H. MEETING MANAGEMENT GOALS

Formal BsUFA meetings between sponsors and FDA consist of Biosimilar Initial Advisory and BPD Type 1–4 meetings. These meetings are further described below.

A Biosimilar Initial Advisory Meeting is an initial assessment limited to a general discussion regarding whether licensure under section 351(k) of the Public Health Service Act may be feasible for a particular product, and, if so, general advice on the expected content of the development program. Such term does not include any meeting that involves substantive review of summary data or full study reports. Only one BIA meeting may be granted per program. While preliminary comparative analytical data from at least one lot of the proposed biosimilar or interchangeable product compared to the U.S.-licensed reference product is not required for the meeting request, sufficient information should be provided with the meeting request to enable FDA to make such a preliminary determination related to potential licensure under section 351(k) and to provide meaningful advice. This should include, as appropriate:

Identification of reference product.

The indications intended to be sought for licensure.

A comparative analytical similarity plan, including preliminary identification of the Critical Quality Attributes and planned characterization methods.

If a sponsor seeks to utilize a non-US-licensed comparator during development, the proposed bridging strategy for US-licensed reference product and that comparator should be provided.

A conceptual plan for non-clinical studies or rationale and justification of why such studies may not needed.

A conceptual description of the planned clinical pharmacokinetics and/or pharmacodynamic study(ies), including proposed endpoints.

If the sponsor plans to conduct a comparative clinical safety and efficacy study, a conceptual plan should be provided. This would include the patient population and proposed endpoints.

Any guidance already received from other health authorities on product development.

Identification to the FDA of the regulatory status in other jurisdictions.

A BPD Type 1 Meeting is a meeting which is necessary for an otherwise stalled drug development program to proceed (e.g. meeting to discuss clinical holds, dispute resolution meeting), a special protocol assessment meeting, or a meeting to address an important safety issue.

A BPD Type 2a Meeting is a meeting focused on a narrow set of issues (e.g., often one, but not more than two issues and associated questions), requiring input from no more than 3 disciplines or review divisions. In order to request a Type 2a meeting, sponsors must first have had a BIA or other BPD meeting with the Agency. Requests could include:

Defined CMC post-approval commitments (e.g., related to analytical methods) discussing the approach in advance of conducting the study to ensure the approach is in line with the Agency's expectations.

Imunogenicity testing strategy following prior FDA recommendations/feedback.

Feedback on revised study design when revisions are based on prior FDA feedback.

A BPD Type 2b Meeting is a meeting to discuss a specific issue (e.g., proposed study design or endpoints) or questions where FDA will provide advice regarding an ongoing biosimilar biological product development program. This meeting may include substantive review of summary data, but does not include review of full study reports.

A BPD Type 3 Meeting is an in depth data review and advice meeting regarding an ongoing biosimilar biological product development program. This meeting includes substantive review of full study reports, FDA advice regarding the similarity between the proposed biosimilar biological product and the reference product, and FDA advice regarding additional studies, including design and analysis.

A BPD Type 4 Meeting is a pre-submission meeting to discuss the format and content of a complete application for an original biosimilar biological product application under the Program or supplement submitted under 351(k) of the PHS Act. The purpose of this meeting is to discuss the format and content of the planned submission and other items, including identification of those studies that the sponsor is relying on to support a demonstration of biosimilarity or interchangeability, discussion of any potential review issues identified based on the information provided, identification of the status of ongoing or needed studies to adequately to address the Pediatric Research Equity Act (PREA), acquainting FDA reviewers with the general information to be submitted in the marketing application (including technical information), and discussion of the best approach to the presentation and formatting of data in the marketing application.

1. Response to Meeting Requests

a. Procedure: FDA will notify the sponsor in writing of the date, time, and place for the meeting, as well as expected Center participants following receipt of a formal meeting request and background package. Table 1 below indicates the timeframes for FDA's response to a meeting request.

TABLE 1

Meeting Type	Response Time (calendar days)
Biosimilar Initial Advisory	21
BPD Type 1	14
BPD Type 2a, 2b, 3 and 4	21

i. For Biosimilar Initial Advisory and BPD Type 2a or 2b meetings, the sponsor may request a written response to its questions, rather than a face-to-face meeting or teleconference. If a written response is deemed appropriate, FDA will notify the sponsor of the date it intends to send the written response. This date will be consistent with the timeframes specified in Table 2 below for the specific meeting type.

ii. For the BPD Type 2a meeting, 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. When it is determined that the meeting request can be appropriately addressed through a written response, FDA will notify the sponsor 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 timeframe for a Type 2a meeting. If the sponsor believes a face-to-face Type 2a meeting is valuable and warranted, then the sponsor may provide a rationale in a follow-up correspondence explaining why a face-to-face meeting is valuable and warranted, and FDA will reconsider this request. If FDA agrees to grant the face-to-face format, the Agency will strive to schedule the meeting to occur within 60 days of FDA's receipt of the meeting request.

b. Performance Goal: FDA will respond to meeting requests and provide notification within the response times noted in Table 1 for 90 percent of each meeting type.

2. 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 in Table 2. Table 2 below indicates the timeframes for FDA to schedule the meeting following receipt of a formal meeting request and background package, or in the case of a written response for Biosimilar Initial Advisory and BPD Type 2a and 2b meetings, 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 2

Meeting Type	Meeting Scheduling or Written Response Time
Biosimilar Initial Advisory.	75 calendar days from receipt of meeting request and background package
BPD Type 2a	60 calendar days from receipt of meeting request and background package
BPD Type 2b	90 calendar days from receipt of meeting request and background package
	Meeting Scheduling Time
BPD Type 1	30 calendar days from receipt of meeting request and background package
BPD Type 3	120 calendar days from receipt of meeting request and background package
BPD Type 4	60 calendar days from receipt of meeting request *

*Note the background package for BPD Type 4 meetings must be received no later than 14 calendar days after FDA receipt of the meeting request.

b. Performance goal:

TABLE 3

Meeting Type	Goal
BPD Type 2a	FY 2023: 50% of meetings are held or written responses are sent within the timeframe FY 2024: 60% of meetings are held or written responses are sent within the timeframe FY 2025: 70% of meetings are held or written responses are sent within the timeframe FY 2026: 80% of meetings are held or written responses are sent within the timeframe FY 2027: 90% of meetings are held or written responses are sent within the timeframe
Biosimilar Initial Advisory and BPD Type 2b.	90% of meetings are held or written responses are sent within the timeframe
BPD Type 1, 3, and 4	90% of meetings are held within the timeframe for each meeting type

3. Preliminary Responses

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 face-to-face or teleconference meeting date for BPD Type 2b and Type 3 meetings.

b. Performance goal:

TABLE 4

Meeting Type	
BPD Types 2b and 3	90% of preliminary responses to questions are issued by FDA no later than five calendar days before the meeting date

4. Meeting Minutes

a. Procedure: The Agency will prepare minutes which will be available to the sponsor 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 in bulleted form and need not be in great detail. Meeting minutes are not necessary if the Agency transmits a written response for Biosimilar Initial Advisory, BPD Type 2a, or 2b meetings.

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

5. Conditions: For a meeting to qualify for these performance goals:

a. A written request and supporting documentation (i.e., the background package) must be submitted to the appropriate review division or office. The background package must be submitted at the same time as the written request for Biosimilar Initial Advisory, BPD Type 1, 2a, 2b and 3 meetings. For BPD Type 4 meetings, the background package must be received no later than 14 calendar days after FDA receipt of the written request.

b. The request must provide:

i. A brief statement of the purpose of the meeting, the sponsor's proposal for the type of meeting, and the sponsor's proposal for a face-to-face meeting, teleconference, or for a written response (Biosimilar Initial Advisory and BPD Type 2a and 2b meetings only);

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

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

iv. A list of questions, grouped by discipline (For each question there should be a brief explanation of the context and purpose of the question);

v. A listing of planned external attendees; and

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

vii. Suggested dates and times (e.g., morning or afternoon) for the meeting that are within or beyond the appropriate time frame of the meeting type being requested.

c. The Agency concurs that the meeting will serve a useful purpose (i.e., it is not premature or clearly unnecessary). However, requests for BPD Type 2b, 3, and 4 Meetings will be honored except in the most unusual circumstances.

The Center may determine that a different type of meeting (i.e., Biosimilar Initial Advisory, or BPD Type 1–4) is more appropriate and it may grant a meeting of a different type than requested, which may require the payment of a biosimilar biological product development fee as described in section 744H of the Federal Food, Drug, and Cosmetic Act before the meeting will be provided. If a biosimilar biological product development fee is required under section 744H, and the sponsor does not pay the fee within the time frame required under section 744H, the meeting will be canceled. If the sponsor pays the biosimilar biological product development fee after the meeting has been cancelled due to non-payment, the time frame described in section I.I.1.a will be calculated from the date on which FDA received the payment, not the date on which the sponsor originally submitted the meeting request.

Sponsors are encouraged to consult available FDA guidance to obtain further information on recommended meeting procedures.

6. Guidance, Clarity, and Transparency

a. Guidance: By September 30, 2023, FDA will issue a revised draft of the existing draft guidance on ''Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products'' with information pertaining to BIA, Type 2a, and Type 4 meetings, as well as the follow-up opportunity described below. 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 will develop criteria and parameters for permissible requests, and 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.

c. Transparency: On or before March 31st, 2025, FDA will publish on its public webpage certain metrics regarding the new Type 2a meeting and sponsor requests for face-to-face meetings for year 1 and year 2 of BsUFA III.

II. ENHANCING BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCT DEVELOPMENT AND REGULATORY SCIENCE

To facilitate the timely development of biosimilar and interchangeable biological products and their availability to patients, FDA will focus on enhancing communications during application review, including inspection communications, and advancing the development of combination and interchangeable products. FDA will also pilot a regulatory science program focused on enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar and interchangeable biological development.

A. PROMOTING BEST PRACTICES IN COMMUNICATION BETWEEN FDA AND SPONSORS DURING APPLICATION REVIEW

The utilization of best practices in communication during application review are the responsibility of both industry and FDA. Efforts from both industry and FDA are needed

in order to continue advancement, improvement, and updating of best practices.

To continue to enhance communication with sponsors during biosimilar application review in BsUFA III, FDA will update relevant guidances, MAPPs and SOPPs, as appropriate, on or before December 31st, 2023 regarding best practices in communication. FDA will utilize input from the BsUFA II final assessment of the Program, FDA experiences, and discussion from a meeting with industry on best practices in FY 2022 to update the above documents, as appropriate.

B. INSPECTIONS AND ALTERNATIVE TOOLS TO EVALUATE FACILITIES

1. Enhancing Inspection Communication for Applications, not Including Supplements

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

When FDA determines for an application, not including supplements, that it is necessary to conduct a pre-license 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 the pre-license inspection 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.

2. Alternative Tools to Assess Manufacturing Facilities Named in Pending Applications

During the COVID–19 public health emergency, the FDA expanded its use of alternate tools for assessing facilities named in applications, including exercising its authority to request records and other information in advance of or in lieu of an inspection, granted per section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 374(a)). Where appropriate, the Agency also increased the use of information, including inspection reports, shared by trusted foreign regulatory partners through mutual recognition agreements and other confidentiality agreements. As FDA continues to gain experience and lessons learned from the use of these tools, FDA will communicate its thinking on the use of such methods beyond the pandemic.

On or before September 30, 2023, FDA will issue draft guidance on the use of alternative tools to assess manufacturing facilities named in pending applications (e.g., requesting existing inspection reports from other trusted foreign regulatory partners through mutual recognition and confidentiality agreements, requesting information from applicants, requesting records and other information directly from facilities and other inspected entities, and, as appropriate, utilizing new or existing technology platforms to assess manufacturing facilities). The guidance will incorporate best practices, including those in existing published documents, from the use of such tools during the COVID–19 pandemic. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

C. ADVANCING THE DEVELOPMENT OF BIOSIMILAR BIOLOGICAL-DEVICE COMBINATION PRODUCTS REGULATED BY CDER AND CBER

1. 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 biosimilar biologic-device combination product. FDA will establish the following procedures for review of URRAs for combination products:

a. 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.

b. 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.

c. URRA submission: performance goals for FDA will be phased in, starting FY 2024 as follows:

i. By FY 2024, review and notify sponsor of agreement or non-agreement with comments for 50% of filed submissions, within 60 days of receipt of submission.

ii. By FY 2025, review and notify sponsor of agreement or non-agreement with comments for 70% of filed submissions, within 60 days of receipt of submission.

iii. By FY 2026, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.

iv. By FY 2027, review and notify sponsor of agreement or non-agreement with comments for 90% of filed submissions, within 60 days of receipt of submission.

d. On or before the end of FY 2024, FDA will publish new draft or revised guidance for review staff and industry describing considerations related to biosimilar biologic-device combination products on the topics noted below.

Guidance will convey FDA's current thinking regarding how a URRA along with other information can be used to inform when the results from an HF validation study may need to be submitted to a marketing application. The guidance will provide a comprehensive, systematic and stepwise approach with examples, when applicable, to illustrate how to make this determination.

e. Sponsors may still elect to submit a URRA with a HF validation protocol and will only be subject to timelines in Section II.C.2., For Human Factor Validation Study Protocols.

2. Human Factor Validation Study Protocols

Human factors studies are conducted to evaluate the user interface of a biosimilar 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:

a. 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).

b. 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:

c. Beginning in FY 2023, review and provide sponsor with written comments for 90% of human factors validation protocol submissions within 60 days of receipt of protocol submission.

D. ADVANCING DEVELOPMENT OF INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCTS

FDA is committed to a focused effort to further advance the development of safe and effective interchangeable biosimilar biological products. The effort will address current needs, prospectively identify future needs and incorporate the following components:

1. Research: FDA will leverage the BsUFA III Regulatory Science Program to advance product development, assist regulatory decision-making, and support guidance development for interchangeable biosimilar products.

2. Foundational guidance development: FDA will develop foundational guidances for the development of interchangeable biosimilar biological products:

a. On or before September 30, 2025, FDA will publish a draft guidance describing considerations for developing presentations, container closure systems and device constituent parts for proposed interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

b. On or before September 30, 2023, FDA will publish draft guidance on labeling for interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

c. On or before September 30, 2024, FDA will publish a draft guidance on promotional

labeling and advertising considerations for interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It will then work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

d. On or before September 30, 2024, FDA will publish a draft guidance on the nature and type of information, for different reporting categories, a sponsor should provide to support post-approval manufacturing changes to approved biosimilar and interchangeable biosimilar biological products. FDA will work towards the goal of publishing final guidance within 18 months after the close of the public comment period on the draft guidance. If, after receiving comments on the draft guidance, FDA determines that the guidance requires substantive changes on which further public comments are warranted, FDA will issue a revised draft guidance within those 18 months instead. It then will work towards publishing a final guidance within 18 months after the close of the public comment period on the revised draft guidance.

3. Stakeholder Engagement: FDA will hold a scientific workshop on the development of interchangeable products to help identify future needs (e.g., guidance, research) on or before October 31, 2025. Within 12 months following the public workshop, FDA will issue a draft strategy document for public comment that outlines the specific actions the agency will take to facilitate the development of interchangeable biosimilar biological products. The strategy document may identify activities and deliverables including updating or creating new procedures, MAPPs, SOPPs, guidances, and other changes to FDA's scientific and other programs related to the topics discussed in the workshop. The strategy document will also include proposed timeframes for the specific actions outlined in the document. FDA will consider public input and will publish a final strategy document within 9 months after the close of the public comment period on the draft strategy document.

E. REGULATORY SCIENCE TO ENHANCE THE DEVELOPMENT OF BIOSIMILAR AND INTERCHANGEABLE BIOLOGICAL PRODUCTS

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development. Starting in FY 2023, FDA will pilot a regulatory science program broadly applicable to facilitating biosimilar and interchangeable biological product development. Project goals should not be specific to a product or product class. The pilot program will focus on two demonstration projects: (1) advancing the development of interchangeable products, and (2) improving the efficiency of biosimilar product development.

1. Advancing Development of Interchangeable Products

This demonstration project will be focused on progressing research to advance the development of interchangeable products. Specifically, this demonstration project will:

a. Investigate and evaluate the data and information (including Real World Evidence) needed to meet the safety standards for determining interchangeability under section 351(k)(4) of the PHS Act, including:

i. Investigate and evaluate informative, scientifically appropriate methodologies to assess the potential impact of differences between proposed interchangeable biosimilar and reference product presentations and container closure systems.

ii. Investigate and evaluate informative, scientifically appropriate methodologies to predict immunogenicity by advancing the knowledge of analytical (including physical, chemical and biological function assays), pharmacological and clinical correlations as relates to interchangeability.

2. Improving the Efficiency of Biosimilar Product Development

This demonstration project will be focused on progressing research to advance the efficiency of biosimilar product development, enhance regulatory decision-making based on the latest scientific knowledge, and advance the use of innovative scientific methodologies and experience with biosimilars. Specifically, this demonstration project will:

a. Review and evaluate opportunities for streamlining and targeting biosimilar product development in consideration of scientific advancements in analytical (including physical, chemical and biological function assays), and pharmacological assessments and experience with prior biosimilar product development and marketed biosimilar products.

b. Investigate and evaluate informative, scientifically appropriate methodologies to predict immunogenicity by advancing the knowledge of analytical (including physical, chemical and biological function assays), pharmacological and clinical correlations as it relates to biosimilarity.

3. Stakeholder Engagement: On or before October 31, 2025, FDA will hold a public meeting to review the progress of the demonstration projects and solicit input on future priorities. An interim report will be posted on FDA's website in advance of the public meeting. On or before September 30, 2027, a final summary report of outcomes from the pilot program will be posted on FDA's website.

4. Deliverables: Within 12 months of the completion of the demonstration projects, FDA will use the learnings from the demonstration projects to publish a comprehensive strategy document outlining specific actions the agency will take to facilitate the development of biosimilar and interchangeable biological products. The comprehensive strategy document may include updating or creating new procedures, MAPPs, SOPPs, and guidances and will also include proposed timeframes for the specific actions outlined in the document. The comprehensive strategy document will be distinct from the final summary report of the pilot program.

III. CONTINUED ENHANCEMENT OF USER FEE RESOURCE MANAGEMENT

FDA is committed to ensuring the sustainability of BsUFA program resources and to enhancing the operational agility of the BsUFA program. FDA will build on the financial enhancements included in BsUFA II and continue activities in BsUFA III to ensure optimal use of user fee resources and the alignment of staff to workload through the continued maturation and assessment of the Agency's resource capacity planning capability. FDA will also continue activities to promote transparency of the use of financial resources in support of the BsUFA program.

A. RESOURCE CAPACITY PLANNING

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

1. Resource Capacity Planning Implementation

a. On or before the end of the 2nd quarter of FY 2023, FDA will publish an implementation plan that will describe how resource capacity planning and time reporting will continue to be implemented during BsUFA III. This implementation plan will address topics relevant to the maturation of resource capacity planning, including, but not limited to, detailing FDA's approach to:

i. The continued implementation of the Agency's resource capacity planning capability, including:

1) The continual improvement of the Capacity Planning Adjustment (CPA); and

2) The continual improvement of time reporting and its utilization in the CPA.

ii. The integration of resource capacity planning analyses in the Agency's resource and operational decision-making processes.

b. FDA will provide annual updates on the FDA website on the Agency's progress relative to activities detailed in this implementation plan on or before the end of the 2nd quarter of each subsequent fiscal year.

c. FDA will document in the annual BsUFA Financial Report how the CPA fee revenues are being utilized.

2. Resource Capacity Planning Assessment

On or before the end of FY 2025, an independent contractor will complete and publish an evaluation of the resource capacity planning capability. This will include an assessment of the following topics:

a. The ability of the CPA to forecast resource needs for the BsUFA program, including an assessment of the scope of the workload drivers in the CPA and their ability to represent the overall workload of the BsUFA program;

b. Opportunities for the enhancement of time reporting toward informing resource needs; and

c. The integration and utilization of resource capacity planning information within resource and operational decision-making processes of the BsUFA program.

The contractor will provide options and recommendations in the evaluation regarding the continued enhancement of the above topics as warranted. The evaluation findings and any related recommendations will be discussed at the FY 2026 BsUFA 5–year financial plan public meeting. After review of the findings and recommendations of the evaluation, FDA will, as appropriate, continue improving the resource capacity planning capability and the CPA.

B. FINANCIAL TRANSPARENCY

1. FDA will publish a BsUFA 5–year financial plan on or before the end of the 2nd quarter of FY 2023. The plan shall recognize that the retention of the strategic hiring and retention adjustment required by section 744H(b)(1)(C) of the FD&C Act is subject to renegotiation under a subsequent reauthorization of BsUFA. FDA will publish updates to the 5–year plan on or before the end of the 2nd quarter of each subsequent fiscal year. The annual updates will include the following topics:

a. The changes in the personnel compensation and benefit costs for the process for the review of biosimilar biological product applications that exceed the amounts provided by the personnel compensation and benefit costs portion of the inflation adjustment; and

b. FDA's plan for managing costs related to strategic hiring and retention after the adjustment required by section 744H(b)(1)C) of the FD&C Act expires at the end of fiscal year 2027, given this adjustment is not intended to be reauthorized in a subsequent reauthorization of BsUFA.

2. FDA will convene a public meeting on or before the end of the 3rd quarter of each fiscal year to discuss the BsUFA 5–year financial plan and the Agency's progress in implementing resource capacity planning, including the continual improvement of the CPA and time reporting, and the integration of resource capacity planning in resource and operational decision-making processes.

C. MANAGEMENT OF CARRYOVER BALANCE

FDA is committed to reducing the carryover balance to no greater than 21 weeks of the target revenue by the end of FY 2025.

In the annual updates to the BsUFA five-year financial plan, FDA will provide updates on its progress towards implementing its plan to reduce the carryover balance as outlined in the FY 2022 BsUFA financial report and the five-year financial plan.

IV. IMPROVING FDA HIRING AND RETENTION OF REVIEW STAFF

Enhancements to the biosimilar biological product review program require that FDA hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of 351

(k) applications. During BsUFA III, the FDA will commit to do the following:

A. SET CLEAR GOALS FOR BIOSIMILAR BIOLOGICAL PRODUCT REVIEW PROGRAM HIRING

1. The BsUFA III agreement provides FDA additional user fee funding to hire additional staff for the biosimilar biological product review program in BsUFA III. FDA will set clear goals to hire the new staff outlined in Table 1.

TABLE 1

	FY 2023	FY 2024	FY 2025	FY 2026	FY 2027
CDER	14	1	0	0	0

2. FDA will report on progress against the hiring goal for BsUFA III on a quarterly basis posting updates to the FDA BsUFA Performance webpage.

B. COMPREHENSIVE AND CONTINUOUS ASSESSMENT OF HIRING AND RETENTION

The Directors of CDER and CBER will utilize a qualified, independent contractor with expertise in assessing HR operations to conduct a targeted assessment of the hiring and retention of staff for the biosimilar biological product review program. The BsUFA III assessment will be conducted under the same contract and by the same independent contractor that will conduct the assessment related to hiring and retention of staff for the human drug review program in PDUFA VII. The contractor will assess the factors that contribute to HR successes and challenges, including factors outside of FDA's control. The assessment will build upon the findings of previous evaluations conducted under BsUFA II and PDUFA VI with a focus on the changes and adjustments that have improved FDA's hiring and retention outcomes and which challenges remain. In addition to evaluating the outcomes of various hiring changes, the assessment will include metrics related to recruiting and retention in the biosimilar biological product review program, including, but not limited to, specific targeted scientific disciplines, attrition, and utilization of pay authorities. The report will include the contractor's findings and recommendations on further enhancements to hiring and retention of staff for the biosimilar biological product review program, if warranted.

The assessment will be published on FDA's website on or before June 30th, 2025 for public comment. FDA will also hold a public meeting on or before September 30th, 2025 to discuss the report, its findings, and the Agency's specific plans to address the report recommendations.

V. INFORMATION TECHNOLOGY GOALS

Under BsUFA III, FDA will:

A. DEVELOP DATA AND TECHNOLOGY MODERNIZATION STRATEGY

FDA will progress a Data and Technology Modernization Strategy (''Strategy'') that provides FDA's strategic direction for current and future state data-driven regulatory initiatives.

1. No later than Q4 FY 2023, FDA will establish a Data and Technology Modernization Strategy that reflects the vision in FDA's Technology and Data Modernization Action Plans, including:

a. outlining key areas of focus and approach including leveraging cloud technologies to support Applicant-FDA regulatory interaction;

b. articulating enterprise-wide approaches for both technology and data governance; and

c. aligning strategic initiatives in support of BsUFA review goals, drawing a line of sight between initiatives and the enterprise strategy (i.e. the agency-wide strategy also supporting components outside BsUFA).

2. The Strategy will be shared and annually updated to reflect progress and any needed adjustments. Milestones and metrics for BsUFA initiatives will be included in the updates.

B. MONITOR AND MODERNIZE ELECTRONIC SUBMISSION GATEWAY (ESG)

FDA will continue to ensure the usability and improvement of the ESG.

1. Annually, FDA will provide on the ESG website historic and current metrics on ESG performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.

FDA will advance the ESG cloud-based modernization with an improved architecture that supports greatly expanding data submission bandwidth and storage, while continuing to ensure its stable operation.

2. Annually, FDA will provide on the ESG website historic and current metrics on ESG performance in relation to published targets, characterizations and volume of submissions, and standards adoption and conformance.

3. By the end of FY 2025, FDA will complete ESG transition to the cloud, including set-up and integration of an enterprise Identity and Access Management solution that will streamline applicant access to FDA resources.

4. Annually, FDA will share progress against the implementation project plan.

5. FDA will engage industry to provide feedback and/or participate in pilot testing in advance of implementing significant changes that impact industry's interaction with the enterprise-wide systems.

VI. DEFINITIONS AND EXPLANATION OF TERMS

A. 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.

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

RECOGNIZING THE 38TH ANNIVERSARY OF ANTI-SIKH VIOLENCE IN INDIA

Mr. TOOMEY. Mr. President, as a proud member of the American Sikh Congressional Caucus, I would like to join my Sikh friends in Pennsylvania's Sikh community and Sikhs around the world in recognizing the 38th anniversary of the November 1984 anti-Sikh violence in India.

For those of you who are not familiar, Sikhism traces its nearly 600-year history to the Punjab region of India. With nearly 30 million followers globally and 700,000 here in the U.S., Sikhism is one of the world's major religions.

Historically, Sikhs have showcased a commitment to serving individuals from all religious, cultural, and ethnic backgrounds—demonstrating their generosity and deep sense of community. During the COVID–19 pandemic, Sikh communities across Pennsylvania and the United States came together to deliver groceries, masks, and other supplies to tens of thousands of families in need no matter their race, gender, religion, or creed. In my many years serving the Commonwealth, I have personally witnessed the spirit of Sikhs and have come to better understand the Sikh tradition that is founded on equality, respect, and peace. It is clear that the presence and contributions of Sikh communities have thoroughly enriched their neighborhoods across the country.

1984 marks one of the darkest years in modern Indian history. The world watched as several violent incidents broke out among ethnic groups in India, with several notably targeting the Sikh community. Today we are here to remember the tragedy that commenced on November 1, 1984, following decades of ethnic tension between Sikhs in the Punjab province and the central Indian Government. As so often in such cases, the official estimates likely do not tell the whole story, but it is estimated that over 30,000 Sikh men, women, and children were deliberately targeted, raped, slaughtered, and displaced by mobs across India.

To prevent future human rights abuses, we must recognize their past forms. We must remember the atrocities committed against Sikhs so that those responsible may be held accountable and that this type of tragedy is not repeated against the Sikh community or other communities across the globe.

ADDITIONAL STATEMENTS

100 YEARS OF THE LEBANON AMERICAN CLUB IN DANBURY, CONNECTICUT

● Mr. BLUMENTHAL. Mr. President, today I rise to recognize the Lebanon American Club of Danbury, CT, as they celebrate 100 years of devoted cultural engagement and civic service in their community.

The Lebanon American Club—or ''the Club,'' as it is affectionately known as by its members—was founded in 1922 as