FY 2019

PERFORMANCE REPORT
TO
CONGRESS

for the

Generic Drug User Fee Amendments

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Commissioner's Report

I am pleased to present to Congress the Food and Drug Administration's (FDA or the Agency) fiscal year (FY) 2019 performance report on the Generic Drug User Fee Amendments (GDUFA) program. This report details FDA's preliminary accomplishments in FY 2019 (October 1, 2018, through September 30, 2019) and updates FDA's performance for the previous year of GDUFA. This report marks the second year of the Generic Drug User Fee Amendments of 2017, also referred to as "GDUFA II."

Over the course of the GDUFA program, FDA has reduced review times for new generic drug applications, approved a record number of generic drug applications, and met or exceeded most of the performance goals while maintaining the Agency's high approval standards. Under GDUFA II, this success has been greatly augmented by the performance goals and program enhancements specified in the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Commitment Letter[1]), which targets aspects of the generic drug review program that are important for facilitating timely access to quality, affordable medicines.

Complementing the performance goals and program enhancements agreed to in GDUFA II, FDA's Drug Competition Action Plan (DCAP[2]) was launched in 2017 to further promote competition and access to affordable generic drug products. Under DCAP, FDA has focused efforts on three key areas: (1) improving the efficiency of the generic drug development, review, and approval process; (2) maximizing scientific and regulatory clarity with respect to complex generic drug products (such products generally are more difficult to genericize, e.g., they have a complex active ingredient or a complex device component); and (3) closing loopholes that allow brand-name drug companies to "game" FDA rules in ways that delay the generic competition Congress intended.

We are confident that the new processes introduced through GDUFA II and activities taken under DCAP will continue to help reduce review cycles, to improve approval times, and to boost competition, helping to ensure that safe, effective, high-quality generic drug products are available to the American public.

I am excited about FDA's significant progress in meeting the challenges and responsibilities of the generic drug program. I look forward to continued engagement with the generic drug industry, Congress, and other stakeholders.

Stephen M. Hahn, M.D.
Commissioner of Food and Drugs

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[1] https://www.fda.gov/media/101052/download.
[2] https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan.

Acronyms

ANDA – Abbreviated New Drug Application

API – Active Pharmaceutical Ingredient

BE – Bioequivalence

CC – Controlled Correspondence

CBER – Center for Biologics Evaluation and Research

CDER – Center for Drug Evaluation and Research

CGMP – Current Good Manufacturing Practice

CGT - Competitive Generic Therapy

CR – Complete Response

CRL - Complete Response Letter

DMF – Drug Master File

DRL – Discipline Review Letter

eCTD – Electronic Common Technical Document

EU – European Union

FDA – Food and Drug Administration

FDARA – FDA Reauthorization Act of 2017

FDASIA – Food and Drug Administration Safety and Innovation Act

FD&C Act – Federal Food, Drug, and Cosmetic Act

FDF – Finished Dosage Form

FY – Fiscal Year (October 1 to September 30)

GDUFA – Generic Drug User Fee Amendments

GDUFA I – Generic Drug User Fee Amendments of 2012

GDUFA II - Generic Drug User Fee Amendments of 2017

IA – Import Alert

IR – Information Request

IT – Information Technology

IVPT – In Vitro Permeation Test

MAPP – Manual of Policies and Procedures

MDI – Metered Dose Inhaler

MRA – Mutual Recognition Agreement

NAI – No Action Indicated

OAI – Official Action Indicated

OGD – Office of Generic Drugs

PAI – Pre-Approval Inspection

PAS – Prior Approval Supplement

PBPK – Physiologically-Based Pharmacokinetic

PFC – Pre-Submission Facility Correspondence

PK – Pharmacokinetic

RLD – Reference Listed Drug

RPM – Regulatory Project Manager

RTR – Refuse to Receive

TA – Tentative Approval

UL – Untitled Letter

VAI – Voluntary Action Indicated

WL – Warning Letter

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Executive Summary

On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA),[3] which included the authorization of the Generic Drug User Fee Amendments of 2012 (GDUFA I). GDUFA I authorized the Food and Drug Administration (FDA or the Agency) to collect user fees for human generic drug activities and enabled FDA to advance a safer, more efficient, and more affordable human generic drug review program.

On August 18, 2017, the President signed into law the FDA Reauthorization Act of 2017 (FDARA),[4] which included the Generic Drug User Fee Amendments of 2017 (GDUFA II). FDA worked closely with the generic drug industry during the development of GDUFA II to enhance the success started under GDUFA I with two main areas of focus: reducing the number of review cycles to approval and increasing approvals of safe, high-quality, and lower-cost generic drugs. This work included identifying opportunities for earlier and enhanced communication to support the efficient and effective pre-market review of generic drugs. Such communication is critical for FDA to meet the new, shorter review goals negotiated under GDUFA II for generic drug submissions that are public health priorities. These communication enhancements and shorter review goals are supported by an overall user fee structure that is consistent with FDA's anticipated workload and public health priorities.

Another key feature unique to GDUFA II is the pre-abbreviated new drug application (pre-ANDA) program, which was designed to support development of complex generic drug products.[5] The pre-ANDA program features Product Development, Pre-Submission, and Mid-Review Cycle meetings to help clarify regulatory expectations early in product development and during application review.

As described in this report, these and many other elements of the GDUFA II program have produced success for the generic drug program, but more importantly, success for the American patient. This annual report presents preliminary data on FDA's success in meeting fiscal year (FY) 2019 review goals and commitments for GDUFA II and updates the data for FY 2018.

Highlighted Achievements – FY 2019

FDA has made noteworthy advancements in the implementation of GDUFA II in a number of areas. Highlights of these activities are provided below.

Generic Drug Assessment and Approval Activity Highlights:

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[3] www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf.

[4] www.congress.gov/115/plaws/publ52/PLAW-115publ52.pdf.

[5] See the definition of "complex product" in Appendix A.

In FY 2019, FDA approved 935 abbreviated new drug applications (ANDAs) and tentatively approved 236 ANDAs.

A critically important subset of these generic drug approvals is the category of "first generics." These products are uniquely important to public health because they represent the first generic drugs approved for a brand-name drug. Every approved generic potentially means more affordable treatment options for patients, and a first approved generic opens the door to that access for the first time. To facilitate access to these products, FDA prioritizes review of submissions for potential first generics. Significant first generic approvals for FY 2019 include clobazam tablets and capsules (reference listed drug (RLD) is Onfi), buprenorphine transdermal system (RLD is Butrans), lurasidone tablets (RLD is Latuda), and Wixela Inhub (RLD is Advair Diskus). A list of all first-time generic approvals[6] for each calendar year is posted on www.FDA.gov.

FDA also is increasing approval of products for which there is insufficient generic drug competition under the new competitive generic therapy (CGT) process established in FDARA. In this process, FDA designates and expedites the development and review of ANDAs for drug products for which there is inadequate competition. *Competitive Generic Therapies*,[7] a draft guidance for industry published in February 2019, details the process an applicant can follow to request CGT designation and the Agency's criteria for designating a drug as a CGT, as well as other information about this important pathway to generic drug approval. To further incentivize competition for these drugs, FDARA created a new type of 180-day exclusivity for the first approved applicant of a drug with a CGT designation for which there were no unexpired patents or exclusivities listed in the Orange Book at the time of original submission of the ANDA.[8]

In FY 2019, 14 generic drug products (in 11 ANDAs) were approved with CGT exclusivity, with an average time to market after approval of 11 days. The successful implementation of the CGT pathway demonstrates that it is efficient and effective at promoting new competition from new generic drug products.

Pre-ANDA Program Highlights:

As part of GDUFA II, FDA committed to a new pre-ANDA program to assist applicants in developing more complete submissions, promote a more efficient and effective ANDA review process, and reduce the number of review cycles and facilitate approval of complex generic drug products. This program is showing strong signs of success. For example, during FY 2019, FDA facilitated 76 pre-ANDA meetings for prospective applicants, published 141 product-specific guidances (PSGs) for complex products, and addressed 1,232 controlled correspondence (CC) for complex products. Pre-ANDA program[9] information is posted on FDA.gov. Additional details on this important program are provided below in this report.

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[6] www.fda.gov/drugs/drug-and-biologic-approval-and-ind-activity-reports/first-generic-drug-approvals.

[7] www.fda.gov/media/125134/download.

[8] CGT is the subject of an article and podcast on CDER's Small Business and Industry Assistance website: www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/competitive-generic-therapies-may-23-2019-issue.

[9] www.fda.gov/industry/generic-drug-user-fee-amendments/pre-anda-program-complex-generic-products.

Review Efficiency Highlights:

Under GDUFA II, FDA committed to review and act on 90 percent of a number of submission types, including:

- FDA agreed to review and act on standard original ANDAs within 10 months of the date of ANDA submission (i.e., a 10-month goal date). As of September 30, 2019, FDA has met 97 percent of the FY 2019 goal for these applications.

- FDA agreed to review and act on priority original ANDA submissions with an 8-month goal date. As of September 30, 2019, FDA met 100 percent of the FY 2019 goal for these applications.

- FDA agreed to review and act on standard prior approval supplements (PASs) and met 98 percent of that goal.

In addition, to improve the predictability, transparency, and efficiency of the review process, as well as to minimize the number of review cycles leading to approval, FDA also agreed in GDUFA II to issue communications related to ANDA deficiencies during the course of the review of original ANDAs. FDA continues to embrace these mechanisms. As of September 30, 2019, FDA issued 4,162 information requests (IRs) and 2,997 discipline review letters (DRLs). These and other important activities are posted in the Activities Report of the Generic Drugs Program (FY 2019) Monthly Performance[10] on www.FDA.gov.

ANDA Development and Review Support Activities Highlights:

FDA's commitments under GDUFA II were not limited to direct ANDA assessment activities. For example, under GDUFA II, FDA committed to review and respond to 90 percent of all standard CC within 60 days of the date of submission and 90 percent of all complex CC within 120 days of the date of submission. FDA received 3,206 CCs during FY 2019, a number that has tripled since the beginning of GDUFA. Even with the substantial increase, as of September 30, 2019, FDA continues to exceed the GDUFA II goals with a 99 percent timely response rate for all standard CC and a 97 percent response rate for all complex CC.

FDA's efforts to increase review efficiency also has been greatly enhanced by the Agency's publication of guidances for industry on a number of important topics related to generic drug development and assessment. FDA publishes guidances to share the Agency's current thinking and recommendations to industry on specific topics, including generic drug development, pharmaceutical quality, regulatory review, and ANDA approval processes. In FY 2019, FDA

[10] www.fda.gov/drugs/abbreviated-new-drug-application-anda/activities-report-generic-drugs-program-fy-2019-monthly-performance.

issued six final and nine draft guidances for industry related to generic drugs, not including PSGs discussed below.[11] Final guidances issued in FY 2019 were published for:

- ANDA Submissions – Content and Format of Abbreviated New Drug Applications
- Determining Whether to Submit an ANDA or a 505(b)(2) Application
- Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA
- Child-Resistant Packaging Statements in Drug Product Labeling
- Questions and Answers on Current Good Manufacturing Practices—Laboratory Controls
- Data Integrity and Compliance with Drug CGMP Questions and Answers

Draft and revised draft guidances were published for generic drug products including:

- Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs
- Assessing Adhesion with Transdermal Delivery Systems and Topical Patches for ANDAs
- ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs
- Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format
- Competitive Generic Therapies
- Using the Inactive Ingredient Database
- Quality Considerations for Continuous Manufacturing
- CDER's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality
- Harmonizing Compendial Standards with Drug Application Approval Using the USP Pending Monograph Process

In addition to these general guidances, FDA published 107 new draft guidances and 145 revised draft guidances with product-specific recommendations in FY 2019. These draft PSGs describe the Agency's current thinking and draft recommendations on how to develop generic drug products that are therapeutically equivalent to specific RLDs.

Regulatory and Scientific Outreach Activities Highlights:

FDA engaged in significant outreach efforts to educate and inform industry participants and other stakeholders about GDUFA II and the generic drugs program. During FY 2019, FDA held six regulatory science public meetings and workshops including: The FDA/DIA Complex Generic Drug-Device Combination Products Workshop 2018 (October 2018); Workshop: Flight Simulator: Learning How to Develop Complex Generic Drug Products (November 2018); FDA and ASCPT Co-Sponsored ASCPT 2019 Pre-conference: PBPK Modeling for the Development and Approval of Locally Acting Drug Products (March 2019); the Center for Drug Evaluation and Research (CDER) Small Business and Industry Assistance (SBIA) Regulatory Education for Industry (REdI) Generic Drug Forum (April 2019), which drew more than 2,230 registrants from 73 countries; FY 2019 Generic Drug Regulatory Science Initiatives Public Workshop (May 2019); and the 2019

[11] www.fda.gov/regulatory-information/search-fda-guidance-documents.

CDER SBIA REdI[12] Complex Generic Drug Product Development Workshop (September 2019). In its second year, the 2019 CDER SBIA REdI Complex Generic Drug Product Development Workshop drew approximately 2,000 participants (18 percent more than the 2018 workshop). In this and other science-focused workshops, FDA communicated to the generic industry how FDA research outcomes guide and facilitate complex generic drug product development. The annual Generic Drug Regulatory Science Initiatives Public Workshop provided an overview of the current status of the regulatory science initiatives for generic drugs and, as a part of GDUFA commitments, solicited public input on research priorities in various topic areas to develop an annual list of regulatory science initiatives specific to generic drugs. FDA took the information it obtained from the public workshop into account in developing the FY 2020 GDUFA Science and Research Priority Initiatives (Appendix B).

During FY 2019, experts from the Office of Generic Drugs also presented in two SBIA REdI Webinars: Financial Incentives for CDER Medical Products (June 2019)[13] and How should I measure this? An FDA perspective on the Bioanalytical Method Validation (BMV) (June 2019).[14]

In addition to these outreach activities, FDA-supported regulatory science research under GDUFA II produced 72 peer-reviewed publications related to generic drugs. See the discussion of "Significant FY 2019 Research Accomplishments" in this report for examples of publications related to research.

Also, as part of its GDUFA II commitments, FDA posted the FY 2018 GDUFA Science and Research Outcomes.[15] This website provides a list of all the research outcomes for the fiscal year in one easily accessible place and fulfills FDA's commitment to annually report the extent to which GDUFA regulatory science-funded projects support the development of generic drug products, the generation of evidence needed to support efficient review and timely approval of ANDAs, and the evaluation of generic drug equivalence. These outcomes are also included in the FY 2018 GDUFA Science and Research Report.[16] The website and report provide greater public transparency regarding the important work the generic drug program engages in to advance the science of generic drugs and provide generic drug developers, applicants, and FDA reviewers essential tools and information to help expedite the availability of high-quality, lower-cost, safe, and effective generic drugs.

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[12] www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/sbia-conferences-and-workshops. [13] www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/regulatory-education-industry-redi-webinar-financial-incentives-cder-medical-products-june-10-2019.

[13] www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/regulatory-education-industry-redi-webinar-financial-incentives-cder-medical-products-june-10-2019.

[14] www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/regulatory-education-industry-redi-how-should-i-measure-fda-perspective-bioanalytical-method.

[15] www.fda.gov/drugs/generic-drugs/fy-2018-gdufa-science-and-research-outcomes?utm_campaign=SBIA%3A%20FDA%20publishes%20FY2018%20GDUFA%20Science%20and%20Research%20Outcomes&utm_medium=email&utm_source=Eloqua.

[16] www.fda.gov/drugs/generic-drugs/office-generic-drugs-fy-2018-gdufa-science-and-research-report.

These and the many additional activities described in this report demonstrate that the generic drug program under GDUFA II is as strong as it has ever been and that FDA is fully committed to maximizing its success to help ensure that safe, effective, high-quality generic drug products are available to the American public.

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Introduction

Millions of Americans use generic drugs to treat a wide variety of medical conditions.[17] The Food and Drug Administration (FDA) helps ensure that human generic drug products are thoroughly tested and shown to meet the statutory standards for approval, generally with evidence that they contain the same active ingredients, route of administration, labeling, strength, and dosage form; are bioequivalent, e.g., deliver the same amount of active ingredients to the site of action; and maintain the same strict standards of good manufacturing practice regulations as their brand-name counterparts.[18]

The Generic Drug User Fee Amendments (GDUFA) authorizes FDA to collect user fees to support human generic drug activities.

Since the implementation of GDUFA in FY 2012 (GDUFA I), FDA has met or exceeded a majority of its goals while maintaining its high standards for generic drug products regarding safety, quality, and transparency. GDUFA has provided the mechanism necessary to secure the resources needed to gain efficiencies, promote innovation, and enhance the overall generic drug review process.

On August 18, 2017, the President signed the FDA Reauthorization Act of 2017[19] into law, which included GDUFA II. Under GDUFA II, FDA is continuing to modernize the generic drug program by improving the program's efficiency, quality, and predictability. GDUFA II provides an opportunity for generic drug applications that are public health priorities to receive a shorter review goal date. For example, applications for drug products that are not blocked by patents or market exclusivities are prioritized if there are not more than three FDA-approved applications for such drug products. This policy supports competition for drug products with limited competition.

GDUFA II also includes increased communication and collaboration between FDA and industry to help improve the quality of submissions and identify, earlier in the process, potential issues that could impact approval of an application. For example, under GDUFA II, FDA issues information requests (IRs) or discipline review letters (DRLs) during the review of an original abbreviated new drug application (ANDA) (1) when further information or clarification is needed or would be helpful to allow completion of a discipline review or (2) to convey preliminary thoughts on possible deficiencies, respectively. These tools allow applicants to address some issues within the original review cycle so that approval or tentative approval (TA) within the first cycle is more achievable.

GDUFA II also introduced a pre-ANDA program designed to support development of complex generic drug products, which features Product Development, Pre-Submission, and Mid-Review

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[17] According to a report compiled by the QuintilesIMS Institute on behalf of the Association for Accessible Medicines, generic drugs saved the American health care system almost $2 trillion over the 10-year period from 2007 through 2017—with over $265.1 billion saved in 2017 alone. The report is available at https://accessiblemeds.org/sites/default/files/2018_aam_generic_drug_access_and_savings_report.pdf.

[18] Some generic drugs are permitted, after grant of a suitability petition, to deviate in minor ways from the innovator they copy. See section 505(j)(2)(C) of the Federal Food, Drug, & Cosmetic Act.

[19] www.congress.gov/115/plaws/publ52/PLAW-115publ52.pdf.

Cycle Meetings to help clarify regulatory expectations early in product development and during application review.

Under GDUFA II, FDA is also taking steps to foster earlier development of guidance, including product-specific guidances (PSGs), which are intended to share the Agency's thoughts on key aspects that should be addressed in related ANDA submissions. Providing timely guidance to generic drug developers allows the applicants to build the Agency's recommendations into their research and development programs and helps them submit higher quality ANDAs. This results in fewer deficiencies in applications submitted to FDA, which should lead to more first cycle approvals.

Performance Presented in This Report

GDUFA commitments cover a wide range of improvements including enhancing communication between FDA and industry throughout the review process, enhancing communications regarding inspections of facilities and sites, improving predictability and transparency, promoting the efficiency and effectiveness of the review process, enhancing drug master file (DMF) reviews, enhancing accountability and reporting, and advancing regulatory science initiatives. This report details FDA's preliminary performance in the second year of GDUFA II and presents the Agency's progress in accomplishing the FY 2018 program goals and enhancements of GDUFA II. Unless otherwise noted, all preliminary data for FY 2019 are as of September 30, 2019.
The information below provides some key terms and concepts used in this report.

- FDA will annually report GDUFA performance data for each fiscal year receipt cohort (defined as submissions received from October 1 to September 30). Some submissions received in FY 2019 may have associated goals in the subsequent fiscal year. In these cases, FDA's performance will be reported in the subsequent fiscal year.
- In GDUFA II, amendments are considered part of the cohort for the fiscal year in which the amendment is submitted. For instance, an amendment submitted in FY 2018 to an original application that FDA received in FY 2016 would be in the FY 2018 cohort under GDUFA II. This is a change from GDUFA I where amendments were considered part of the cohort for the fiscal year for the original submission to which the amendment is updating. For instance, an amendment submitted in FY 2017 (GDUFA I) to an original application that FDA received in FY 2016 would be in the FY 2016 cohort under GDUFA I. The longest goal date in the FY 2018 cohort is 10 months, and under the GDUFA II paradigm for determining cohort year of amendments, the cohort will be completely closed or "mature" 10 months after the last day of the cohort fiscal year (except that ANDAs and amendments that get extensions, typically because of unsolicited amendments, may have a goal date occurring more than 10 months after the last day of the cohort fiscal year). Therefore, the FY 2018 cohort "matured" on July 31, 2019.
- As part of GDUFA II, FDA committed to "continue to work through the goal date if, in FDA's judgment, continued work would likely result in an imminent TA that could prevent forfeiture of 180-day exclusivity or in an imminent approval" (section II(B)(6) of the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022

(GDUFA II Commitment Letter)[20]). There have been numerous instances in which the Agency worked past a goal date rather than issuing a complete response letter (CRL) by the goal date to resolve outstanding issues with the ANDA and issued an approval or TA. As a result of these efforts under this program enhancement commitment, FDA has reduced the number of review cycles necessary for approval of these applications and facilitated more timely access to generic drug products.

- For a review goal to be met, FDA must review the specified percentage of submissions within the review goal. For example, in FY 2019, to meet the goal for standard original ANDAs, FDA must review and act on 90 percent of them within 10 months.
- To "act on an application" means that FDA will issue a CRL, an approval letter, a TA letter, or a refuse to receive (RTR) letter.
- Submission types with shorter review goals (e.g., standard and priority minor ANDA amendments with 3-month goal dates) tend to have a larger percentage of reviews completed by the end of the fiscal year, and their preliminary performance is a more reliable indicator of their final performance. However, submission types (e.g., standard original ANDA submissions) with longer review goals (e.g., 10-month goal date in FY 2019) tend to have a smaller percentage of reviews completed by the end of the fiscal year, and their preliminary performance is a less reliable indicator of their final performance.

Definitions of key terms used throughout this report can be found in Appendix A.

[20] https://www.fda.gov/media/101052/download.

GDUFA Review Workload

The table below summarizes GDUFA workload for FY 2018 and presents preliminary workload data for FY 2019.

GDUFA II Workload	FY 2018*	FY 2019
Original ANDAs		
Total Original ANDAs Submitted	1,044	911
ANDAs Submitted After RTR for Failure to Pay User Fees	16	14
ANDAs Submitted After RTR for Technical Reasons	81	51
ANDA Solicited Amendments		
Total Solicited ANDA Amendments Submitted	2,330	2,275
Prior Approval Supplements (PASs)		
Total PAS Submissions	1,103	890
PAS Solicited Amendments		
Total Solicited PAS Amendments Submitted	160	197
DMF		
Total DMFs Submitted	344	273
Controlled Correspondence (CC)		
Total CC Submitted	2,933	2,937

**Numbers were changed to reflect updates to data presented in the FY 2018 GDUFA Performance Report.*

GDUFA Review Goals

Under GDUFA I, different cohorts and tiers of submissions had different goals. GDUFA II changed the review goal structure. In GDUFA II, most goal dates are measured against a 90 percent metric, and there are different review times for standard and priority ANDA submissions. This new scheme not only streamlines the process but promotes more predictable timelines for actions.

GDUFA II Review Goals – FY 2019 Preliminary Performance

The table below reflects the ANDA review goals for FYs 2018 to 2022.

GDUFA II Review Goals by Submission Type	Review and Act on % Within	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
Original ANDA Review*						
Standard Original ANDA Submissions	10 months	90%	90%	90%	90%	90%
Priority Original ANDA Submissions (if applicant meets requirements of a Pre-Submission Facility Correspondence (PFC))	8 months	90%	90%	90%	90%	90%
Priority Original ANDA Submissions (if applicant does not meet the requirements of a PFC)	10 months	90%	90%	90%	90%	90%
Amendment Review						
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	90%	90%	90%	90%	90%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	90%	90%	90%	90%	90%
Standard and Priority Minor ANDA Amendments	3 months	90%	90%	90%	90%	90%
PAS Review Time†						
Standard PAS (if pre-approval inspection is not required)	6 months	90%	90%	90%	90%	90%
Standard PAS (if pre-approval inspection is required)	10 months	90%	90%	90%	90%	90%
Priority PAS (if pre-approval inspection is not required)	4 months	90%	90%	90%	90%	90%
Priority PAS (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority PAS (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	90%	90%	90%	90%	90%
PAS Amendments						
Standard Major PAS Amendment (if pre-approval inspection is not required)	6 months	90%	90%	90%	90%	90%
Standard Major PAS Amendment (if pre-approval inspection is required)	10 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if pre-approval inspection is not required)	4 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	90%	90%	90%	90%	90%
Standard and Priority Minor PAS Amendments	3 months	90%	90%	90%	90%	90%
Unsolicited ANDA and PAS Amendments±						
Unsolicited ANDA and PAS Amendments (In Cycle) §	Review and act on unsolicited ANDA amendments and PAS amendments submitted during the review cycle by the later of the goal date for the original submission/solicited amendment or the goal date specifically assigned to the unsolicited amendment. An unsolicited amendment goal date is assigned in the same manner as the corresponding solicited amendment goal date.					
Unsolicited ANDA and PAS Amendments (Between Cycles) §	Review and act on unsolicited ANDA amendments and PAS amendments submitted between review cycles by the later of the goal date for the subsequent solicited amendment or the goal date specifically assigned to the unsolicited amendment. An unsolicited amendment goal date is assigned in the same manner as the corresponding solicited amendment goal date.					

* GDUFA II Commitment Letter - I(A)
† GDUFA II Commitment Letter - I(B)
± GDUFA II Commitment Letter - I(C)
§ For FY 2018, "during the review cycle" and "between review cycles" goals were separate; for FY 2019, they are combined.

GDUFA II also provides new review goals for certain drug master file (DMF) commitments and CC. The table below reflects these review goals for FYs 2018 to 2022.

GDUFA II Goals/Commitment Type	Review-Time Goal	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
DMF						
Complete the initial completeness assessment review of Type II Active Pharmaceutical Ingredient (API) DMFs	Within 60 calendar days of the later of the date of DMF submission or DMF Fee payment	90%	90%	90%	90%	90%
CC ‡‡						
Standard CC	Within 60 calendar days of submission date	90%	90%	90%	90%	90%
Complex CC	Within 120 calendar days of submission date	90%	90%	90%	90%	90%
Submitter requests to clarify ambiguities in the CC	Within 14 calendar days of request receipt	90%	90%	90%	90%	90%

‡‡In the case of CC that raises an issue that relates to one or more pending citizen petitions, the 60- or 120-day timeframe starts on the date FDA responds to the petition (if there is only one petition) or last pending petition.

The following tables represent FDA's FY 2018 updated performance and FY 2019 preliminary performance. FDA continues to meet or exceed most of the review goals for the FY 2018 and 2019 cohorts. The "percent on time" column in the preliminary performance table for FY 2019 shows the percentage of submissions reviewed on time as of September 30, 2019, excluding action pending within the GDUFA review goal, and the "potential range" column shows the potential for meeting the FY 2019 GDUFA review goal.

Both tables also include two columns to reflect review metrics when FDA applied the GDUFA II Commitment Letter's imminent approval program enhancement to qualifying ANDAs. In accordance with the GDUFA II Commitment Letter, FDA may continue to work through the goal date if, in FDA's judgment, continued work would likely result in an imminent TA that could prevent forfeiture of 180-day exclusivity or in an imminent approval. FDA considers an action to be an imminent approval action if an approval or TA occurs within 60 days of the goal date. These imminent approval performance numbers reflect FDA's decision to achieve an approval or TA within 60 days of the goal date rather than act on the goal date, e.g., issue a CRL.

GDUFA FY 18 Updated Review Goals by Submission Type	Review and Act on 90 % Within	Actions Complete†	Percent on Time‡	Potential Range§	On Time Imminent Approval	Imminent Approval Potential Range
Original ANDA Review						
Standard Original ANDA Submissions	10 months	575 of 598	96%	93% to 96%	98%	94% to 98%
Priority Original ANDA Submissions (if applicant meets requirements of a PFC)	8 months	35 of 35	100%	100% to 100%	100%	100% to 100%
Priority Original ANDA Submissions (if applicant does not meet requirements of a PFC)	10 months	407 of 411	97%	96% to 97%	98%	97% to 98%
Amendment Review						
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	744 of 753	96%	95% to 96%	98%	97% to 98%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	35 of 37	100%	95% to 100%	100%	95% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	282 of 284	95%	95% to 95%	98%	98% to 98%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	1 of 1	100%	100% to 100%	100%	100% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	10 of 10	100%	100% to 100%	100%	100% to 100%
Standard and Priority Minor ANDA Amendments	3 months	1244 of 1247	91%	91% to 91%	98%	98% to 98%
Unsolicited ANDA Amendments (In Cycle)	Varies	205 of 210	96%	94% to 96%	---	---
Unsolicited ANDA Amendments (Between Cycles)	Varies	22 of 22	95%	95% to 95%	---	---
PAS Review Time						
Standard PAS (if pre-approval inspection is not required)	6 months	687 of 690	98%	98% to 98%	98%	98% to 98%
Standard PAS (if pre-approval inspection is required)	10 months	32 of 32	97%	97% to 97%	97%	97% to 97%
Priority PAS (if pre-approval inspection is not required)	4 months	47 of 47	98%	98% to 98%	100%	100% to 100%
Priority PAS (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	---	---	---	---	---
Priority PAS (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	6 of 6	83%	83% to 83%	83%	83% to 83%
PAS Amendments						
Standard Major PAS (if pre-approval inspection is not required)	6 months	49 of 49	98%	98% to 98%	98%	98% to 98%
Standard Major PAS (if pre-approval inspection is required)	10 months	---	---	---	---	---
Priority Major PAS (if pre-approval inspection is not required)	4 months	9 of 9	89%	89% to 89%	89%	89% to 89%
Priority Major PASs (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	---	---	---	---	---
Priority Major PASs (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	---	---	---	---	---
Standard and Priority Minor PAS Amendments	3 months	110 of 110	97%	97% to 97%	100%	100% to 100%
Unsolicited PAS Amendments (In Cycle)	Varies	13 of 13	100%	100% to 100%	---	---
Unsolicited PAS Amendments (Between Cycles)	Varies	---	---	---	---	---
DMF						
Complete the initial completeness assessment review of Type II API DMF	60 calendar days	470 of 470	93%	93% to 93%	---	---

GDUFA FY 18 Updated Review Goals by Submission Type	Review and Act on 90 % Within	Actions Complete†	Percent on Time‡	Potential Range§	On Time Imminent Approval	Imminent Approval Potential Range
CC						
Standard CC	60 calendar days	2,780 of 2,781	99%	99% to 99%	---	---
Complex CC	120 calendar days	148 of 149	97%	97% to 97%	---	---
Clarification of Ambiguities in CC Response	14 calendar days	27 of 27	96%	96% to 96%	---	---

GDUFA FY 19 Preliminary Review Goals by Submission Type	Review Time Goal	Actions Complete†	Percent on Time‡	Potential Range§	On Time Imminent Approval	Imminent Approval Potential Range
Original ANDA Review						
Standard Original ANDA Submissions	10 months	112 of 557	97%	20% to 99%	100%	20% to 100%
Priority Original ANDA Submissions (if applicant meets requirements of a PFC)	8 months	19 of 39	100%	49% to 100%	100%	49% to 100%
Priority Original ANDA Submissions (if applicant does not meet requirements of a PFC)	10 months	50 of 243	100%	21% to 100%	100%	21% to 100%
Amendment Review						
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	270 of 846	98%	32% to 99%	100%	32% to 100%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	16 of 38	100%	42% to 100%	100%	42% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	165 of 286	95%	57% to 97%	98%	57% to 99%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	1 of 3	100%	33% to 100%	100%	33% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	5 of 16	100%	31% to 100%	100%	31% to 100%
Standard and Priority Minor ANDA Amendments	3 months	804 of 1,079	92%	69% to 94%	98%	74% to 99%
Unsolicited ANDA Amendments (In Cycle)	Varies	462 of 693	91%	63% to 94%	---	---
Unsolicited ANDA Amendments (Between Cycles)*	Varies	---	---	---	---	---
PAS Review Time						
Standard PAS (if pre-approval inspection is not required)	6 months	464 of 760	98%	60% to 99%	99%	61% to 100%
Standard PAS (if pre-approval inspection is required)	10 months	10 of 31	100%	32% to 100%	100%	32% to 100%
Priority PAS (if pre-approval inspection is not required)	4 months	45 of 67	98%	67% to 99%	98%	67% to 99%
Priority PAS (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	0 of 1	---	0% to 100%	---	0% to 100%
Priority PAS (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	2 of 6	100%	33% to 100%	100%	33% to 100%
PAS Amendments						
Standard Major PAS (if pre-approval inspection is not required)	6 months	30 of 56	100%	54% to 100%	100%	54% to 100%
Standard Major PAS (if pre-approval inspection is required)	10 months	0 of 2	---	0% to 100%	---	0% to 100%
Priority Major PAS (if pre-approval inspection is not required)	4 months	11 of 15	100%	73% to 100%	100%	73% to 100%
Priority Major PASs (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	---	---	---	---	---

GDUFA FY 19 Preliminary Review Goals by Submission Type	Review Time Goal	Actions Complete†	Percent on Time‡	Potential Range§	On Time Imminent Approval	Imminent Approval Potential Range
Priority Major PASs (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	0 of 1	---	0% to 100%	---	0% to 100%
Standard and Priority Minor PAS Amendments	3 months	92 of 117	96%	75% to 97%	97%	76% to 97%
Unsolicited PAS Amendments (In Cycle)	Varies	12 of 14	92%	86% to 93%	---	---
Unsolicited PAS Amendments (Between Cycles)*	Varies	---	---	---	---	---
DMF						
Complete the initial completeness assessment review of Type II API DMF	60 calendar days	394 of 431	95%	87% to 96%	---	---
CC						
Standard CC	60 calendar days	2,567 of 2,983	99%	85% to 99%	---	---
Complex CC	120 calendar days	158 of 212	98%	73% to 99%	---	---
Clarification of Ambiguities in CC Response	14 calendar days	45 of 47	98%	94% to 98%	---	---

***** Starting in FY 2019, in cycle and between cycle unsolicited amendments will be grouped and reported together.
† Actions completed include any action taken regardless of whether it met the review-time goal.
‡ "Percent on time" represents the current percentage of actions FDA completed within the review-time goal.
§ "Range" represents the minimum (all pending become late) and maximum (all pending reviewed on time) performance.

GDUFA II ANDA Review Program Enhancement Goals

Under GDUFA II, FDA committed to several program enhancement goals to improve predictability and transparency, promote efficiency and effectiveness of the review process, minimize the number of review cycles necessary for approval, increase the overall rate of approval, and facilitate greater access to generic drug products. The table below reflects these program enhancement goals for FYs 2018 to 2022.

	Goal	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
Dispute Resolution						
FDA will respond to appeals above the Division level	Within 30 calendar days of the Center for Drug Evaluation and Research's (CDER) receipt of the written appeal pursuant to the applicable goal	70%	80%	90%	90%	90%
Product Development Meetings						
FDA will grant or deny Product Development Meeting Requests	Within 30 calendar days from receipt of request	90%	90%	—	—	—
	Within 14 calendar days from receipt of request	—	—	90%	90%	90%
FDA will conduct Product Development Meetings granted	Within 120 calendar days of granting them	60%	70%	80%	90%	90%
Unless FDA is providing a written response to satisfy the meeting goal, FDA will aspire to provide preliminary written comments before each Product Development Meeting	5 calendar days before the meeting	-	-	-	-	-
FDA will provide meeting minutes	Within 30 calendar days following the meeting	-	-	-	-	-
Pre-Submission Meetings						
FDA will grant or deny Pre-Submission Meeting Requests	Within 30 calendar days from receipt of request	90%	90%	-	-	-
	Within 14 calendar days from receipt of request	-	-	90%	90%	90%
FDA will conduct Pre-Submission Meetings granted	Within 120 calendar days of granting them	60%	70%	80%	90%	90%
If appropriate to the purpose of the meeting, FDA will provide preliminary written comments	5 calendar days before each meeting	-	-	-	-	-
FDA will provide meeting minutes	Within 30 calendar days of the meeting	-	-	-	-	-
DMF First Cycle Review Deficiency						
FDA will strive to grant DMF first cycle review deficiency teleconferences	Within 30 calendar days	-	-	-	-	-
Review Classification Changes During Review Cycle						
FDA will notify the applicant if the review classification of the ANDA or PAS changes from standard to priority during a review cycle of an ANDA or PAS	Within 14 calendar days of the date of the change	-	-	-	-	-

	Goal	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
FDA will notify the applicant if a previous ANDA or ANDA amendment was subject to priority review but a subsequent ANDA amendment is subject to a standard review	Within 14 calendar days of the date of receipt of the solicited amendment	-	-	-	-	-
FDA will decide whether to reclassify a major amendment or standard review status	Within 30 calendar days of date of FDA's receipt of the request for a reclassification	90%	90%	90%	90%	90%
Post-CRL						
FDA will provide a scheduled date for a requested Post-CRL teleconference	Within 10 calendar days of the request for a teleconference	90%	90%	90%	90%	90%
FDA will conduct requested Post-CRL teleconferences on the FDA-proposed date	Within 30 calendar days of the receipt of the written request	90%	90%	90%	90%	90%
Safety Determination Letters						
FDA will issue safety determination letters	Within 60 calendar days of the date of submission of disclosure authorization	90%	90%	90%	90%	90%

Preliminary Performance – FY 2019

The following tables represent FDA's FY 2018 updated and FY 2019 preliminary performance on the GDUFA II program enhancement goals. Program enhancement goals differ from review goals in that "review goals" directly pertain to the review of a generic drug submission, whereas "program enhancement goals" are goals for activities that support generic drug review and approval in general. For example, one of FDA's review goals under GDUFA II is to review and act on 90 percent of standard original ANDAs within 10 months of the date of ANDA submission. The goals for Pre-Submission Meetings below are examples of program enhancement goals. Pre-Submission Meetings are not directly related to the review of a generic drug submission; however, it is important that FDA meet its Pre-Submission Meeting goals and other program enhancement goals to support efficient reviews and more generic drug approvals.

GDUFA II FY 2018 Updated Performance*	Review Goal	Goal	Actions Completed†	Percent on Time‡	Potential Range§
Dispute Resolution					
FDA will respond to appeals above the Division level	Within 30 calendar days of CDER's receipt of the written appeal pursuant to the applicable goal	70%	35 of 35	97%	97% to 97%
Product Development Meetings					
FDA will grant or deny Product Development Meeting Requests	Within 30 calendar days from receipt of request	90%	71 of 71	99%	99% to 99%
FDA will conduct Product Development Meetings granted	Within 120 calendar days of granting them	60%	45 of 45	100%	100% to 100%
Unless FDA is providing a written response to satisfy the meeting goal, FDA will aspire to provide preliminary written comments before each Product Development Meeting	5 calendar days before the meeting	-	35 of 35	100%	100% to 100%
FDA will provide meeting minutes	Within 30 calendar days following the meeting	-	21 of 21	100%	100% to 100%
Pre-Submission Meetings					
FDA will grant or deny Pre-Submission Meeting Requests	Within 30 calendar days from receipt of request	90%	12 of 12	100%	100% to 100%
FDA will conduct Pre-Submission Meetings granted	Within 120 days of granting them	60%	5 of 5	100%	100% to 100%
If appropriate to the purpose of the meeting, FDA will provide preliminary written comments	5 calendar days before each meeting	-	4 of 4	75%	75% to 75%
FDA will provide meeting minutes	Within 30 calendar days of the meeting	-	3 of 3	100%	100% to 100%
DMF First Cycle Review Deficiency					
FDA will strive to grant DMF first cycle review deficiency teleconferences	Within 30 calendar days	-	16 of 16	69%	69% to 69%
Review Classification Changes During Review Cycle					
FDA will notify the applicant if the review classification of the ANDA or PAS changes from standard to priority during a review cycle of an ANDA or PAS	Within 14 calendar days of the date of the change	-	23 of 23	100%	100% to 100%
FDA will notify the applicant if a previous ANDA or ANDA amendment was subject to priority review but a subsequent ANDA amendment is subject to a standard review	Within 14 calendar days of the date of receipt of the solicited amendment	-	24 of 24	92%	92% to 92%

GDUFA II FY 2018 Updated Performance*	Review Goal	Goal	Actions Completed†	Percent on Time‡	Potential Range§
FDA will decide whether to reclassify a major amendment or standard review status	Within 30 calendar days of date of FDA's receipt of the request for a reclassification	90%	195 of 198	99%	96% to 99%
Post-CRL					
FDA will provide a scheduled date for a requested Post-CRL teleconference	Within 10 calendar days of the request for a teleconference	90%	56 of 56	91%	91% to 91%
FDA will conduct requested Post-CRL teleconferences on the FDA-proposed date	Within 30 calendar days of the receipt of the written request	90%	56 of 56	100%	100% to 100%
Safety Determination Letters					
FDA will issue safety determination letters	Within 60 calendar days of the date of submission of disclosure authorization	90%	5 of 5	100%	100% to 100%

* Numbers were changed to reflect updates to data presented in the FY 2018 GDUFA Performance Report.
† Actions completed include any action taken regardless of whether it met the review-time goal.
‡ "Percent on time" represents the current percentage of actions FDA completed within the review-time goal.
§ "Range" represents the minimum (all pending become late) and maximum (all pending reviewed on time) performance.

GDUFA II FY 2019 Preliminary Performance	Review Goal	Goal	Actions* Completed	Percent on Time†	Potential Range‡
Dispute Resolution					
FDA will respond to appeals above the Division level	Within 30 calendar days of CDER's receipt of the written appeal pursuant to the applicable goal	80%	9 of 11	100%	82% to 100%
Product Development Meetings					
FDA will grant or deny Product Development Meeting Requests	Within 30 calendar days from receipt of request	90%	102 of 102	100%	100% to 100%
FDA will conduct Product Development Meetings granted	Within 120 calendar days of granting them	70%	59 of 71	100%	83% to 100%
Unless FDA is providing a written response to satisfy the meeting goal, FDA will aspire to provide preliminary written comments before each Product Development Meeting	5 calendar days before the meeting	-	31 of 47	100%	66% to 100%
FDA will provide meeting minutes	Within 30 calendar days following the meeting	-	20 of 24	100%	83% to 100%
Pre-Submission Meetings					
FDA will grant or deny Pre-Submission Meeting Requests	Within 30 calendar days from receipt of request	90%	10 of 10	100%	100% to 100%
FDA will conduct Pre-Submission Meetings granted	Within 120 days of granting them	70%	5 of 5	100%	100% to 100%
If appropriate to the purpose of the meeting, FDA will provide preliminary written comments	5 calendar days before each meeting	-	4 of 5	100%	80% to 100%
FDA will provide meeting minutes	Within 30 calendar days of the meeting	-	1 of 3	100%	33% to 100%
DMF First Cycle Review Deficiency					
FDA will strive to grant DMF first cycle review deficiency teleconferences	Within 30 calendar days	-	6 of 6	83%	83% to 83%
Review Classification Changes During Review Cycle					
FDA will notify the applicant if the review classification of the ANDA or PAS changes from standard to priority during a review cycle of an ANDA or PAS	Within 14 calendar days of the date of the change	-	35 of 35	100%	100% to 100%
FDA will notify the applicant if a previous ANDA or ANDA amendment was subject to priority review but a subsequent ANDA amendment is subject to a standard review	Within 14 calendar days of the date of receipt of the solicited amendment	-	207 of 209	94%	94% to 94%
FDA will decide whether to reclassify a major amendment or standard review status	Within 30 calendar days of date of FDA's receipt of the request for a reclassification	90%	159 of 164	96%	93% to 96%
Post-CRL					
FDA will provide a scheduled date for a requested Post-CRL teleconference	Within 10 calendar days of the request for a teleconference	90%	66 of 66	79%	79% to 79%

GDUFA II FY 2019 Preliminary Performance	Review Goal	Goal	Actions* Completed	Percent on Time†	Potential Range‡
FDA will conduct requested Post-CRL teleconferences on the FDA-proposed date	Within 30 calendar days of the receipt of the written request	90%	66 of 66	95%	95% to 95%
Safety Determination Letters					
FDA will issue safety determination letter	Within 60 calendar days of the date of submission of disclosure authorization	90%	3 of 3	67%	67% to 67%

* Actions completed include any action taken regardless of whether it met the review-time goal.
† "Percent on time" represents the current percentage of actions FDA completed within the review-time goal.
‡ **"**Range" represents the minimum (all pending become late) and maximum (all pending reviewed on time) performance.

Additional Activities to Promote Transparency and Enhance Communications

Under GDUFA, FDA committed to increasing transparency and communication between FDA and generic drug developers. In addition to the GDUFA II commitments outlined above, in FY 2019, FDA published many guidances for industry[21] and Manuals of Policies and Procedures (MAPPs)[22] that provide important information for generic drug developers. These efforts support high-quality applications, streamlined application assessments, and ultimately faster generic drug approvals. In FY 2019, FDA published the following guidances for industry and MAPPs:

- Draft guidance for industry: *Assessing Adhesion with Transdermal Systems and Topical Patches for ANDAs*, October 2018
- Draft guidance for industry: *Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs*, October 2018
- Final guidance for industry: *Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA*, December 2018
- Final guidance for industry: *Data Integrity and Compliance with Drug CGMP Questions and Answers*, December 2018
- Draft guidance for industry: *ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs*, January 2019
- Draft guidance for industry: *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format*, January 2019
- Draft guidance for industry: *CDER's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality*, February 2019
- Draft guidance for industry: *Competitive Generic Therapies*, February 2019
- Draft guidance for industry: *Quality Considerations for Continuous Manufacturing*, February 2019
- Final guidance for industry: *Determining Whether to Submit an ANDA or a 505(b)(2) Application*, May 2019
- Final guidance for industry: *ANDA Submissions – Content and Format of Abbreviated New Drug Applications, June 2019*
- Draft guidance for industry: *Using the Inactive Ingredient Database, July 2019*

[21] FDA guidances may be accessed at www.fda.gov/regulatoryinformation/guidances/.

[22] CDER MAPPs may be accessed at www.fda.gov/about-fda/center-drug-evaluation-and-research/cder-manual-policies-procedures-mapp.

- Draft guidance for industry: *Harmonizing Compendial Standards with Drug Application Approval Using the USP Pending Monograph Process*, July 2019
- Questions and Answers on Current Good Manufacturing Practices—Laboratory Controls (added three new questions and answers, numbers 15 to 17), August 2019
- Final guidance for industry: *Child-Resistant Packaging Statements in Drug Product Labeling*, August 2019
- MAPP 5220.8: *Evaluating Requests for and Conducting Product Development and Pre-Submission Pre-ANDA Meetings*, September 2019

Pre-ANDA Program Goals – FY 2019 Preliminary Performance

Under GDUFA, FDA committed to advance scientific efforts to develop new human generic drug products and novel dosage forms. Through its regulatory science initiatives, FDA continues to work on developing tools, standards, and approaches to assess the safety, efficacy, and quality of these products and to facilitate the path of these products to market approval.

One example of FDA's commitment to this program has been its PSGs and recommendations for regulatory submissions (e.g., ANDAs, pre-ANDA meeting requests, CCs). FDA developed and published 252 new and revised draft PSGs in FY 2019 (56 percent were for complex products). The table below shows the PSG breakdown for complex and non-complex drug products.

	Complex Drug Products	Non-Complex Drug Products
Number of new PSGs	23	84
Number of revised draft PSGs	118	27
TOTAL	141	111

These PSGs have provided industry with draft recommendations on the design of bioequivalence (BE) studies and scientific advice pertaining to finished dosage forms (FDFs) and drug substances (APIs) that can be used in the development of generic complex and non-complex drugs.

Since FY 2013, FDA has awarded 155 research contracts and grants. A complete list of FY 2013 through FY 2019 awards can be found at www.fda.gov/GDUFARegScience. The number of new and ongoing grants and contracts by fiscal year is provided in the table below.

Fiscal Year	Number of External Research Contracts and Grants Awarded Using GDUFA Funds	
	New Contracts and Grants	Ongoing Contracts and Grants Receiving Funding
2019	20	25
2018	24	16

Significant FY 2019 Research Accomplishments

In addition to serving as the scientific basis for the development of PSGs and specific pre-ANDA communications, research outcomes from intramural and extramural research are published in peer-reviewed scientific literature and are presented and discussed at major medical and scientific meetings to facilitate the path towards generic drug product development and to contribute to general guidance development. GDUFA research includes the following research programs, each highlighted with a key FY 2019 outcome.

- Ophthalmic Drug Products

In 2019, FDA published results from an ophthalmic absorption model for dexamethasone ophthalmic suspensions that was developed and validated using published and in-house-generated rabbit pharmacokinetic (PK) data. The model simulated the ocular drug PK profiles of dexamethasone formulations that are qualitatively and quantitively similar but have differences in drug particle size, formulation viscosity, and strength. The model described the dose-dependent (0.01 to 0.1 percent) non-linear PK in ocular tissues and illustrated that ocular bioavailability is dictated by the interplay between formulation properties and physiological clearance, through drainage and tear turnover rates in the pre-corneal compartment.[23]

- Complex Mixtures and Peptides

  Peptide impurity profiles of teriparatide drug substance and product were identified using ultra-high-performance liquid chromatography-mass spectrometer (UHPLC-MS). Over 30 impurities were identified and quantified, including 16 impurities above the reporting threshold of 0.05 percent. These impurities could be categorized either as degradation products that accumulated over time or process impurities produced during the manufacturing process. Results from these studies provide a useful benchmark for assessing current and future generic teriparatide applications. These studies also provide insight into the analytical process and analysis necessary to ensure the safety and efficacy of generic peptide drug products.

- Long-Acting Injectables

  Poly (lactic-co-glycolic acid) or PLGA is a biodegradable polymer that is widely used in long-acting injectable products. It is the product component that controls the drug release rate. However, PLGAs are complex in nature, and their properties can be altered during manufacturing, which can make reverse engineering difficult. For example, glucose-star

[23] AAPS J. 21:65 (2019). DOI:10.1208/s12248-019-0334-x.

shaped PLGAs are relatively new and have not been well studied compared to other linear PLGAs. Based on FDA's current understanding, comparative characterization data on polymer molecular weight/weight distribution, monomer ratio, and polymer structure (linear vs. branched) are critical. However, there are no readily available methodologies for evaluating the structure of glucose-PLGAs. In FY 2019, FDA and its collaborators successfully developed and validated an analytical technique using a series of in-house synthesized branched-PLGA standards. The method was used to determine the branching parameters of glucose-PLGA extracted from Sandostatin LAR, as well as glucose-PLGAs obtained from three different suppliers in the United States.[24]

- Complex Injectables and Nanomaterials
  An internal FDA research project focused on developing innovative analytical methods to quantify unencapsulated drug, excipients, and potential impurities in the liposome formulations. This collaborative research with FDA's Office of Regulatory Affairs lab resulted in three publications[25] that will aid the development of generic versions of liposome products.

- Orally Inhaled and Nasal Drug Products
  To address challenges with conducting the comparative clinical endpoint BE study for metered dose inhaler (MDI) products, research projects were conducted to identify and develop more predictive, clinically relevant in vitro methodologies for characterizing the aerosolized particles, their deposition and dissolution, as well as new computational modeling and simulation approaches to correlate these results with the delivered dose measured in vivo. As a result of these research projects, on May 2019, the Agency posted the first PSG for a solution-based MDI product (beclomethasone dipropionate) that provides an option for conducting additional in vitro, in vivo, and/or in silico studies for establishing BE, in lieu of conducting the recommended comparative clinical endpoint BE study, in the context of the weight-of-evidence.[26]

[24] Journal of Controlled Release. (2019): DOI: 10.1016/j.jconrel.2019.03.002.

[25] International journal of pharmaceutics, (2019) 569: 118603; International journal of pharmaceutics, (2019) 569: 118576; and International journal of pharmaceutics (2018) 549 (1-2), 109-114.

[26] www.accessdata.fda.gov/drugsatfda_docs/psg/Beclomethasone%20dipropionate%20Inhalation%20Aerosol%20Metered%20NDA%20207921%20PSG%20Page%20RC%20May%202019.pdf.

- Topical Dermatological Drug Products
  An in vivo dermal open-flow microperfusion study was conducted in human subjects to characterize the dose-response relationship and the influence of potentially confounding factors such as local "cross-talk" between probes in adjacent treatment sites or redistribution of the drug via clearance into the systemic circulation and recirculation into the skin. Six healthy subjects were enrolled in this pilot, single center, open label study. The absence of probe contamination from systemic redistribution and the lack of any substantial "cross-talk" between adjacent test sites indicate that individual probes can monitor the local rate and extent of lidocaine and prilocaine specifically and without interference from different treatments at other sites.

- Locally Acting Physiologically Based Pharmacokinetic (PBPK) Modeling
  FDA scientists continued to collaborate with external experts to develop, evaluate, and improve physiologically based models for the most challenging routes of delivery for generic drug development: ophthalmic,[27] inhalation,[28] and dermal.[29] These models aid generic drug development for these routes and help FDA evaluate new BE approaches for these complex routes of delivery. In FY 2019, a PBPK model that allowed the quantitative description of drug absorption through the skin was utilized to support the approval of a generic topical gel product referencing Voltaren (diclofenac sodium) topical gel 1% for the topical treatment to relieve pain associated with osteoarthritis.

- Quantitative Clinical Pharmacology
  Quantitative Clinical Pharmacology approaches are used to integrate physiological, biological, and drug properties to set up clinically relevant BE criteria, evaluate post-marketing signals on generic switches, and explore alternate BE study designs.[30] Two projects were conducted in FY 2019 to evaluate new approaches for assessment of BE in PK study designs with sparse sampling, e.g., for ophthalmic product BE studies that have only one PK sample per subject. Model-based BE analysis strategies can be used to increase the efficiency of generic drug development and regulatory decision-making.

- Oral Absorption Models and Bioequivalence
  Through a collaboration with the University of Michigan, FDA completed a study that simultaneously measured both the systemic concentration of a drug and the drug

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[27] AAPS J. (2019) **21**(4):65. DOI: 10.1208/s12248-019-0334-x Comput Biol Med. 2018 Jan 1; 92:139-146.

[28] CPT: Pharmacometrics & Systems Pharmacology. 2019;8(6):359-370. Int J Numer Method Biomed Eng. 2018 May;34(5): e2955.

[29] Tsakalozou, E. Physiologically-based Pharmacokinetic Modeling and Simulation Approaches: Best Practices for Regulatory Applications Related to Locally-acting Generic Drugs. Presentation at Complex Generic Drug Product Development Workshop. College Park, MD, Sept. 26, 2019 (https://sbiaevents.com/cgp2019/) https://www.certara.com/2018/03/02/skin-in-the-game-mechanistic-modeling-of-dermal-drug-absorption/?ap%5B0%5D=PBPK.

[30] Clin Pharmacol Ther. (2019) 105(2):338–349. DOI: 10.1002/cpt.1282.

concentration in the gastrointestinal tract. For the first time, an in-depth analysis was performed on a large data set derived from an aspiration/motility study, quantifying the impact of physiology on the systemic behavior of an orally administered drug product in fed state conditions. The data obtained from this study will help FDA develop an in vitro biorelevant dissolution approach and optimize in silico tools in order to predict the in vivo performance of orally administered drug products, especially in fed state conditions.[31]

- Generic Drug Substitution
  Researchers funded by FDA grants published the results of a study that evaluated BE between generic and brand name bupropion hydrochloride modified-release products with different release patterns at a steady state in patients with depression. The results confirmed the BE of bupropion products in patients.[32]

- Abuse-Deterrent Opioid Drug Products
  FDA completed an in vivo nasal PK study on milled oxycodone hydrochloride extended-release tablets. The results showed that particle-size distribution was a significant factor in determining the PK of oxycodone following nasal insufflation. Additionally, drug loss during physical manipulation and drug content in the associated particle size range in the manipulated product are also critical and should be measured in nasal insufflation studies. These findings have complemented FDA's internal research and provided valuable support to regulatory activities, such as pre-ANDA meetings, CC, and ANDA reviews, particularly with respect to characterization of physically manipulated abuse-deterrent formulations, study design, and data analysis for in vivo nasal insufflation studies. The results will aid generic drug developers in conducting such studies following recommendations in the PSGs and FDA's guidance for industry *General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products* (November 2017).

- Data Analytics
  With the development of big data toolsets, FDA conducted time-to-event analysis based on machine learning to predict the time to the first submission of ANDAs referencing new chemical entities.[33] This research is important to inform ANDA workload and to prioritize research efforts. Current efforts focus on the prediction of the ANDA submission number.

- Drug-Device Combinations
  FDA research continued to establish the general utility of an in vitro permeation test (IVPT) methodology to compare heat effects between prospective generic and brand-name transdermal systems. The data will be used to evaluate an in vitro-in vivo correlation between IVPT and serum PK data from human subjects and will help to evaluate the effectiveness of an IVPT study as a tool for comparing the bioavailability of the drug from

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[31] Mol Pharm (2018) 15(12):5454; Mol Pharm (2018) 15(12):5468.

[32] Clin Pharmacol Ther. (2018) 105(5): 1164-1174. DOI: 10.1002/cpt.1309 (https://clinicaltrials.gov/ct2/show/NCT02536105).

[33] Clin Pharmacol Ther. (2019) 106(1):174-181.

various transdermal systems under the influence of heat. The research results can be used by generic drug developers to design transdermal systems that perform the same as the brand product. The results can also be used by FDA to compare brand and generic transdermal products in lieu of in vivo studies, which can increase the efficiency of generic drug development.

FY 2020 GDUFA Regulatory Science Priority Initiatives

Similar to GDUFA I, FDA agreed in the GDUFA II Commitment Letter to consult with industry and the public to create an annual list of regulatory science initiatives specific to research on generic drugs.

On May 1, 2019, FDA held the FY 2019 Generic Drug Regulatory Science Initiatives Public Workshop, which provided an overview of the status of the human generic drug regulatory science program and an opportunity for public input in developing the FY 2020 research priorities. Information obtained during the public workshop and other inputs, e.g., comments to the public docket, were considered in developing the FY 2020 Regulatory Science Plan.[34]

The lists of research initiatives for earlier fiscal years are also available on FDA's website. [35,36,37]

The FY 2020 GDUFA Regulatory Science Priority Initiatives identified were grouped into the following four topic areas:

- Topic A: Complex active ingredients, formulations, or dosage forms
- Topic B: Complex routes of delivery
- Topic C: Complex drug-device combinations
- Topic D: Tools and methodologies for BE and therapeutic equivalence evaluation

A description of these topic areas and priorities is provided in Appendix B.

[34] The list of the FY 2020 research initiatives can be found at www.fda.gov/media/132370/download.

[35] The list of the FY 2017 research initiatives can be found at www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM526900.pdf.

[36] The list of the FY 2018 research initiatives can be found at www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/UCM582777.pdf.

[37] The list of the FY 2019 research initiatives can be found at https://www.fda.gov/media/119040/download.

Drug Safety and Inspections Performance

FDA is committed to maximizing efforts to ensure consistency and transparency regarding inspections.

This section satisfies the annual reporting requirement created by the GDUFA II Commitment Letter for FY 2019 to communicate final facility inspection activities for human generic drugs.

GDUFA II Commitments

In the GDUFA II Commitment Letter, FDA committed to include the following metrics annually as part of the GDUFA Performance Report (identified by the corresponding section of the GDUFA II Commitment Letter):

(g) Number of inspections conducted by domestic or foreign establishment location and inspection type (pre-approval inspection (PAI), current good manufacturing practice (CGMP), BE clinical and BE analytical) and facility type (FDF, API)

(h) Median time from beginning of inspection to Form FDA 483 (483) issuance,

(i) Median time from 483 issuance to Warning Letter (WL), Import Alert (IA), and Regulatory Meeting for inspections with final classification of Official Action Indicated (OAI) or equivalent, and

(j) Median time from the date of the WL, IA, and Regulatory Meeting to the resolution of OAI status or equivalent.

FDA interprets the GDUFA II Commitment Letter as follows:

- It is limited to "GDUFA facilities," which are defined as facilities associated with an ANDA that:
    - Is approved, pending, or has a TA
    - Was withdrawn and/or received a complete response (CR) during the given fiscal year, unless the withdrawn or CR date precedes the inspection start date

- If multiple applications were covered under one unique PAI, this report counts them as one inspection.

- 483,[38] *Inspectional Observations*, is the list of observations of objectionable conditions issued by FDA investigators to the inspected facility's management at the conclusion of an inspection. Inspections not resulting in issuance of a Form FDA 483 are excluded from paragraphs "h," "i," and "j" of the GDUFA II Commitment Letter (section VI(C)(3)). Further, most facilities receiving a 483 are classified as Voluntary Action Indicated (VAI), and no compliance action (WL, IA, or Regulatory Meeting) is taken.

- PAIs of ANDA applications only are counted in this report. If there was a PAI of a new drug application or a biologics license application in a facility that is also identified as a GDUFA facility, that PAI is not counted in this report. A PAI is not always performed at facilities named in pending applications. When performed, the PAI evaluates one or more applications pending approval with FDA. (Note that FDA may inspect facilities associated with an application that are not required to self-identify under GDUFA and that may not be required to register under 21 CFR part 207. Inspections of such facilities are included in the data and analysis provided below because such inspections may impact application decisions.)

- FDA conducts other types of inspections of facilities in which a conclusion of non-compliance may result in delay or denial of application approval. Inspections other than PAIs that can also impact an application's approvability include surveillance and for-cause inspections. The result of a PAI may be a decision that an application is not approvable. Issuance of a WL, addition to an IA, or the holding of a Regulatory Meeting, could follow other types of inspections, though not a PAI alone. For that reason, FDA interprets paragraphs "i" and "j" of the GDUFA II Commitment Letter (section VI(C)(3)) to apply to inspections other than PAIs.

- FDA understands paragraphs "i" and "j" of the GDUFA II Commitment Letter (section VI(C)(3)) to apply, consistent with its terms, to inspections resulting in a WL, addition to an IA, or the holding of a Regulatory Meeting. We note that there are situations in which a surveillance inspection would lead directly to a more serious enforcement action, such as a seizure, injunction, or prosecution, without a WL, IA, or regulatory meeting. Such rare circumstances, if they occur, would not be included.

- BE inspections have Untitled Letters (UL) issued only after an OAI inspection. A UL is not equivalent to a WL and is not included in this report.

This report reflects progress on commitments made in connection with GDUFA II started in 2018. Thus, this report does not include information about events that occurred before FY 2018 except as described below. Accordingly:

- For subparagraphs "g" and "h" of the GDUFA II Commitment Letter (section VI(C)(3)), this report includes an inspection for which the inspection ended in the reporting fiscal year, even if the inspection started before the reporting fiscal year. Multiple products/applications can be covered in one inspection assignment; these are counted as one inspection.

[38] More information about 483 can be found at www.fda.gov/ICECI/Inspections/ucm256377.htm.

- For subparagraph “i” of the GDUFA II Commitment Letter (section VI(C)(3)), this report counts WLs, IAs, and Regulatory Meetings that were issued or held in the reporting fiscal year, even if they are based on an inspection for which the 483 was issued before the reporting fiscal year, provided it was issued during the period covered by the GDUFA II Commitment Letter.
- For subparagraph “j” of the GDUFA II Commitment Letter (section VI(C)(3)), this report counts resolutions of WLs, IAs, and Regulatory Meetings when the resolutions occurred in the reporting fiscal year, even if the WLs, IAs, or Regulatory Meetings were issued or held prior to the reporting fiscal year, provided they were issued or held in or after FY 2018, the effective starting year for GDUFA II reporting.

The table below reflects the number of inspections[39] conducted by domestic or foreign establishment location and inspection type (PAI, CGMP, BE clinical and BE analytical) and facility type (FDF, API, other) associated with a generic application as well as the number of 483s issued with the inspections.

	Location			
Inspection Type	**Domestic**	**Foreign**	**Total***	**Number Issued 483**
PAI (API)**	1	58	59	35
PAI (API/FDF)**	4	25	29	23
PAI (FDF)**	56	107	163	106
PAI (Other)**	22	26	48	24
CGMP (API)	28	157	185	107
CGMP (API/FDF)	17	41	58	40
CGMP (FDF)	108	128	236	177
CGMP (Other)	70	40	110	47
BE Clinical**	57	76	133	19
BE Analytical**	13	42	55	5

*This table may overrepresent the number of unique inspections as some inspection assignments cover both PAI and CGMP inspections.
**Other inspections include facilities such as contract testing laboratories and repackagers.

The following table shows the median time (calendar days) between the start of inspections and the issuance of a 483.

Median Time from Beginning of Inspection to 483 Issuance

User Fee Program	FY 2019 Median Time (Calendar Days)
GDUFA	5

The following table shows the median time (calendar days) between the issuance of a 483 and the issuance of a WL, IA, and date of a Regulatory Meeting. This includes WLs, IAs, and

[39] FDA does not include inspection classification decisions associated with inspections performed by other regulatory inspectorates, such as the European Union (EU) member state inspections that FDA may review in implementing the US-EU Mutual Recognition Agreement. Such inspections are generally surveillance-only type inspections, and the inspections may have been performed and completed well before FDA requested a copy of the inspection report, which would complicate the assessment of median days to review and classification.

Regulatory Meetings that were issued or held in the reporting fiscal year, even if they were based on an inspection for which the 483 was issued before the reporting fiscal year. The same facility may receive multiple compliance actions, for example a WL and an IA, following issuance of a 483. Most facilities receiving a 483 are classified VAI, and no WL, IA, or Regulatory Meeting is issued or held.

Median Time from 483 Issuance to WL, IA, and Regulatory Meeting for Inspections with Final Classification of OAI (or Equivalent)

User Fee Program	FY 2019 Median Time FDA 483 to WL	FY 2019 Median Time FDA 483 to IA	FY 2019 Median Time 483 to Reg. Meeting
GDUFA	196	129	173

The following table shows the median time (calendar days) between the issuance or holding of a WL, IA, and Regulatory Meeting and OAI resolution. "OAI resolution" includes the time to remediate CGMP issues at a site classified as OAI and the time for FDA to re-inspect the facility to confirm whether adequate remediation has taken place. The compliance action is considered resolved when the firm has sufficiently addressed the violations or deviations to allow the site to be reclassified by FDA as VAI or No Action Indicated (NAI), and, in the case of an IA or a WL, the Agency has also removed the facility from the IA or closed the WL. This includes OAI resolution of WLs, IAs, and Regulatory Meetings that were issued or held in the reporting fiscal year. The same facility may receive more than one compliance action, for example a WL and an IA, following issuance of a 483. The OAI finalized date is when the facility was classified as OAI and is different from the date of issuance of a WL, IA, or Regulatory Meeting.

Median Time from Date of WLs, IAs, and Regulatory Meetings to Resolution of OAI Status

User Fee Program	FY 2019 Median Time OAI Finalized to Resolution	FY 2019 Median Time WL to OAI Resolution	FY 2019 Median Time IA to OAI Resolution	FY 2019 Median Time Reg. Meeting to OAI Resolution
GDUFA	420	372	N/A	68

During FY 2019, there were 3 facilities issued a WL, IA, or Regulatory Meeting with OAI resolution occurring in or after FY 2018, the beginning of the GDUFA II reporting period. Two of these facilities were issued WLs, and one had a Regulatory Meeting. Resolution includes the firm addressing the CGMP violations or deviations that resulted in the OAI outcome, as well as reinspection and classification of the site as VAI or NAI, if appropriate.

Significant remediation efforts by the firm to resolve the CGMP issues at a site classified as OAI and subsequent reinspection by FDA to determine if the CGMP issues have been resolved are usually required before reclassification. It is unlikely that a regulatory action (i.e., WL, IA, or Regulatory Meeting) is taken, the firm's remediation efforts are completed, and the facility is reinspected and reclassified within a single fiscal year. In some instances, firms either chose not to remediate or never adequately remediate, and violations observed at their facilities and compliance actions indefinitely remain open.

Inspection Efficiency Enhancements

The Agency has implemented various changes and continues to improve how FDA conducts inspections to verify pharmaceutical quality and has improved transparency and timeliness in determining regulatory outcomes from inspections.[40]

In 2012 with the passage of the Food and Drug Administration Safety and Innovation Act,[41], Congress gave FDA the authority to enter into arrangements with a foreign government or an Agency of a foreign government to recognize foreign inspections, after determining that the foreign government has the capability to conduct inspections in accordance with the Federal Food, Drug, and Cosmetic Act (FD&C Act) (section 809). FDA is currently implementing a mutual recognition agreement (MRA) with the European Union (EU), which allows both parties to rely on our respective surveillance inspections in lieu of performing repetitive inspections of the same facilities. FDA and the EU are now fully implementing the MRA related to drug quality surveillance inspections. FDA accomplished the agreed goal of making a capability determination for all 28 EU member state inspectorates of human drugs, including biologicals, by July 15, 2019. As a result of that accomplishment and as provided for in the MRA, the EU has stopped sampling and testing U.S.-produced drug batches distributed in the EU.

[40] www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm619435.htm.

[41] www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf.

Outreach and Facility Assessment

FDA has completed several commitments under the GDUFA II program to provide greater transparency regarding prioritization and scheduling of inspections, as well as to communicate information following inspections. These efforts include updating FDA's publicly available inspection classifications database, communicating with foreign regulatory authorities regarding the compliance status of establishments, providing information on the Agency's Risk-Based Site Selection Model, and communicating information from inspections that may impact approvability to applicants and facility owners.

As part of this commitment, upon receipt of a request by an establishment physically located in the United States that has been included as part of a marketing application submitted to a foreign regulator, FDA will issue, within 30 days of receipt of the request, a letter to an identified foreign regulator conveying the current CGMP compliance status for the establishment.

- FDA did not meet that goal in FY 2018 by responding within 30 days of receipt to one request issued (one request received).

- FDA partially met that goal in FY 2019 by responding within 30 days of receipt to four requests issued (nine requests received).

FDA is actively pursuing additional resources for this program. However, CGMP declarations are only one of several ways that FDA is enhancing communication and transparency with foreign regulatory authorities regarding the compliance status of establishments in the United States. Foreign regulators can also find the CGMP status of an establishment by checking the inspection classifications database for the most recent inspection classification that is publicly available.

The inspection classifications database provides the most recent classifications based on FDA's final assessments following an inspection of manufacturing facilities for routine surveillance purposes or sites conducting BE/bioavailability studies. FDA updates the database every 30 days. Previously, the Agency updated the database every 180 days and did not include inspection classifications of sites conducting clinical BE/bioavailability studies. The Agency also updated the database to build on its progress implementing the MRA with the EU, and the database now supports inclusion of facility status based on the classification of inspection reports from foreign regulatory authorities.

In FY 2019, FDA also updated two guidelines for investigators and compliance officers, one for pharmaceutical drug quality and pre-approval inspections and another covering in vivo bioequivalence inspections.

GDUFA II - Enhanced Accountability and Reporting

GDUFA II includes several commitments and requirements that are critical to enabling progress toward performance goals for the human generic drug program. These include developing a resource management plan, implementing a modernized time reporting and resource management system, and publishing monthly and quarterly metrics on the FDA website. This section details the status of these activities.

Resource Management Planning and Modernized Time Reporting

FDA committed to conducting activities necessary to fulfill the resource management objectives. FDA has worked diligently to ensure compliance with this undertaking. The following table describes FDA's FY 2018 and FY 2019 commitments and progress in this area.

Activity	Due Date/Deadline	Status
FDA will develop and publish a resource management planning and modernized time reporting implementation plan.	No later than the fourth quarter of FY 2018	FDA published the implementation plan on March 30, 2018
FDA will implement methodologies for assessing resource needs of the program and tracking resource utilization across the program elements.	Following the report review and comments	

Financial Transparency and Efficiency

FDA also agreed to conduct activities to evaluate the financial administration of the GDUFA program to help identify areas to enhance operational and fiscal efficiency.

Activity	Due Date/Deadline	Status
FDA will contract with an independent third party to obtain an evaluation of how the GDUFA program is resourced and how those resources are utilized and to recommend improvements to the process.		FDA published the FY 2018 Human Drug User Fees Financial Management Evaluation in May2019 https://www.fda.gov/drugs/development-resources/fiscal-year-2018-financial-management-evaluation-human-drug-user-fees-assessment-report
FDA will use the results of the evaluation to create an ongoing financial reporting mechanism to enhance the transparency of GDUFA program resource utilization.		In progress
FDA will publish updates to the GDUFA Five-Year Financial Plan.	No later than the 2nd quarter of each subsequent fiscal year	FDA published the FY 2019 GDUFA Five-Year Financial Plan update in May 2019 because of the federal government shutdown.
FDA will convene a public meeting to discuss the GDUFA Five-Year Financial Plan, along with the Agency's progress in implementing modernized time reporting and resource management planning.	No later than the third quarter of each fiscal year starting in FY 2019.	FDA held a public meeting on Financial Transparency and Efficiency of GDUFA in June 2019.

Performance Reporting

In the GDUFA II Commitment Letter, FDA committed to publish monthly and quarterly performance metrics on its website. These metrics can be found on the FDA website at:

www.fda.gov/drugs/abbreviated-new-drug-application-anda/activities-report-generic-drugs-program-fy-2019-monthly-performance and https://www.fda.gov/industry/activities-report-generic-drugs-program-fy-2019-gdufa-ii-quarterly-performance, respectively.

FDA also committed to publishing more performance metrics in the annual GDUFA Performance Report. These further performance metrics have either already been captured in this report or are captured in the tables below.

The following table summarizes FDA's GDUFA II commitment to promote accountability and transparency by providing the mean and median approval times for generic drug reviews for the FYs 2018 and 2019 receipt cohorts. These metrics only include applications approved or tentatively approved at the time this report was prepared. In future reports to Congress, these metrics will be revised to include applications that are approved or tentatively approved in subsequent fiscal years. Thus, the current numbers are a measure of both the earliest and fastest submissions reaching approval. The approval times and numbers of cycles will increase with each re-analysis of the cohort. These re-analyses will be presented in future reports to Congress.

GDUFA II	FY 2018*	FY 2019
Receipt Cohort		
Mean Approval Time (Calendar Days)	371	281
Median Approval Time (Calendar Days)	330	296
Mean Tentative Approval Time (Calendar Days)	431	350
Median Tentative Approval Time (Calendar Days)	399	350
Mean Number of ANDA Review Cycles to Approval	1	1
Median Number of ANDA Review Cycles to Approval	1	1
Mean Number of ANDA Review Cycles to Tentative Approval	2	1
Median Number of ANDA Review Cycles to Tentative Approval	2	1

*Numbers were changed to reflect updates to data presented in the FY 2018 GDUFA Performance Report.

FDA also committed to annual reporting on the following information about the workload managed by the generic drug program.

GDUFA II	FY 2018*	FY 2019
Application Receipt		
Number of Applications Received	960	793
Number of Applications Refused to Receive	89	44
Average Time to Receipt (i.e., number of days) Decision	49	44
ANDA Review		
Number of ANDA Applications Received by FDA for Standard Review	555	522
Number of ANDA Applications Received by FDA for Priority Review	405	271
Percentage of ANDA proprietary name requests reviewed within 180 days of receipt	97%	93%
Petitions		
Number of suitability petitions pending a substantive response for more than 270 days from the date of receipt	136	153
Number of 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	0	0
DMF		
Number of DMF First Adequate Letters issued status (or equivalent)	189	198
Email Exchanges		
Number of initial (first cycle) email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in DMF deficiency letters.	56	63
Number of follow-up email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in follow-up cycle DMF deficiency letters	10	2

*Numbers were changed to reflect updates to data presented in the FY 2018 GDUFA Performance Report.

Management Initiative	Performance Area	FY 2018*	FY 2019
When requested by the ANDA applicant within 10 calendar days of FDA issuing a CRL, FDA will schedule a teleconference to provide clarification concerning deficiencies identified in the CRL.[42]	Teleconferences Requested	72	90
	Teleconferences Granted	56	66
	Teleconferences Denied	16	24
	Teleconferences Conducted	56	66
When requested by the ANDA applicant, FDA will schedule a teleconference to clarify issues and answer questions on reclassifying a major amendment or standard review status.	Teleconferences Requested	30	12
	Teleconferences Granted	24	12
	Teleconferences Denied	0	0
	Teleconferences Conducted	24	8
FDA will offer to hold a Mid-Review Cycle teleconference with an applicant if a Product Development or Pre-Submission Meeting has been held.[43]	Teleconferences Offered	1	4
	Teleconferences Scheduled	1	4
	Teleconferences Conducted	1	1

*Numbers were changed to reflect updates to data presented in the FY 2018 GDUFA Performance Report.

[42] FDA may close out a request for a first cycle CR teleconference by (1) holding the teleconference or (2) responding to questions in the applicant's teleconference request in writing in lieu of holding the teleconference.

[43] The GDUFA II Commitment Letter specifies that FDA will publish metrics on the number of "GDUFA related teleconferences requested, granted, denied and conducted," but these terms do not neatly apply to Mid-Review Cycle Meetings. The more applicable terms, "offered," "scheduled," and "conducted" are used instead.

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Appendices

Appendix A: Definitions of Key Terms

A. **Act on an Application** means that FDA will either issue a CRL, an approval letter, a TA letter, or an RTR action.

B. **Active pharmaceutical ingredient (API)** means:
(i) a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended to be used as a component of a drug and intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or
(ii) a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become the final active pharmaceutical ingredient as defined in paragraph (i).

C. **Amendments to an ANDA** – The GDUFA II Commitment Letter reflects significant changes in the classification of review goals for amendments to ANDAs and PASs from the GDUFA I Commitment Letter. Under GDUFA I, amendments were classified into a complex Tier system based on the following factors: whether the amendment was solicited or unsolicited, whether the amendment was major or minor, the number of amendments submitted to the ANDA or PAS, and whether an inspection was necessary to support the information contained in the amendment. GDUFA II simplified the amendment review goals and no longer subjects them into a Tier system; however, GDUFA II review goals are still dependent on whether the amendment is designated as a standard or priority, whether the amendment is classified as major or minor, and whether or not a pre-approval inspection is needed.

   Descriptions of major and minor amendments were considered during the GDUFA II negotiations and incorporated in the GDUFA II Commitment Letter. FDA's guidance for industry *ANDA Submissions — Amendments to Abbreviated New Drug Applications Under GDUFA* (July 2018) supersedes FDA's guidance for industry *Major, Minor, and Telephone Amendments to Abbreviated New Drug Applications* (December 2001) and, as agreed to during negotiations, incorporates excerpted text describing major and minor amendment types that are contained in Appendix B of the July 2018 guidance. See https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

D. **Abbreviated new drug application (ANDA)** is defined as "the application described under [21 CFR] 314.94, including all amendments and supplements to the application." See 21 CFR 314.3(b).

E. **Bioequivalence (BE)** is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.

F. **Complete response letter (CRL)** refers to a written communication to an applicant or DMF holder from FDA usually describing all 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. CRLs will reflect a complete review, which includes an application-related facilities assessment and will require a complete response from industry to trigger another review cycle with an attendant goal date. Refer to 21 CFR 314.110 for additional details. When a citizen petition may impact the approvability of the ANDA, FDA will strive to identify, where possible, valid issues raised in a relevant citizen petition in the CRL. If a citizen petition raises an issue that would delay only part of a CR, a response that addresses all other issues will be considered a CR.

G. **Complete review** refers to a full division-level review from all relevant review disciplines, including inspections, and includes other matters relating to the ANDAs and associated DMFs, as well as consults with other Agency components.

H. **Complex controlled correspondence (CC)** means:

1. CC involving evaluation of clinical content,

2. BE protocols for reference listed drugs (RLDs) with Risk Evaluation and Mitigation Strategies Elements to Assure Safe Use, or

3. Requested evaluations of alternative bioequivalence approaches within the same study type (e.g., pharmacokinetic, in vitro, clinical).

I. **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 and complex ophthalmological products and otic dosage forms that are formulated as suspensions, emulsions or gels) or complex dosage forms (e.g., transdermals, metered dose inhalers, extended release injectables);

2. Complex drug-device combination products (e.g., auto injectors, 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.

J. **Controlled Correspondence (CC)** is correspondence submitted to the Agency, by or on behalf of a generic drug manufacturer or related industry, requesting information on a specific element of generic drug product development. See the guidance for industry *Controlled Correspondence Related to Generic Drug Development*.[44] CC does not include citizen petitions, petitions for reconsideration, or requests for stay.

K. **Discipline review letter (DRL)** means a letter used to convey preliminary thoughts on possible deficiencies found by a discipline reviewer and/or review team for its portion of the pending application.

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[44] www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm411478.pdf.

L. **Facility** is described as a business or other entity under one management, either direct or indirect, and at one geographic location or address, engaged in manufacturing or processing an API or an FDF, but does not include a business or other entity whose only manufacturing or processing activities are one or more of the following: repackaging, relabeling, or testing.

M. **Finished Dosage Form (FDF)** means:

(i) a drug product in the form in which it will be administered to a patient, such as a tablet, capsule, solution, or topical application;

(ii) a drug product in a form in which reconstitution is necessary prior to administration to a patient, such as oral suspensions or lyophilized powders; or

(iii) any combination of an API with another component of a drug product for purposes of production of such a drug product.

N. **GDUFA** – GDUFA I and GDUFA II

O. **GDUFA I** – Generic Drug User Fee Amendments for Fiscal Years 2013 to 2017

P. **GDUFA II** – Generic Drug User Fee Amendments for Fiscal Years 2018 to 2022

Q. **Information Request (IR)** – means a letter that is sent to an applicant during a review to request further information or clarification that is needed or would be helpful to allow completion of the discipline review.

R. **Mid-Review Cycle Meeting** – A teleconference meeting with the applicant to discuss current concerns with the application and next steps. CDER schedules this teleconference after the last key discipline has issued its IR and/or DR for ANDAs that were the subject of prior Product Development Meetings or Pre-Submission Meetings.

S. **Original ANDA** – The initial submission to FDA's CDER Office of Generic Drugs or Center for Biologics Evaluation and Research (CBER) of an ANDA.

T. **Pre-Submission Meeting** means a meeting in which an applicant has an opportunity to discuss and explain the format and content of an ANDA to be submitted. Although the proposed content of the ANDA will be discussed, Pre-Submission Meetings will not include substantive review of summary data or full study reports.

U. **Prior Approval Supplement (PAS)** means a request to the Secretary to approve a change in the drug substance, drug product, production process, quality controls, equipment, or facilities covered by an approved ANDA when that change has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product.[45]

V. **Priority** means submissions affirmatively identified as eligible for a priority review per section 505(j)(11)(A) of the FD&C Act or CDER's MAPP 5240.3, *Prioritization of the Review of Original ANDAs, Amendments and Supplements*, as revised.

[45] See section 744A(11) of the FD&C Act.

W. **Product Development Meeting** – means a meeting involving a scientific exchange to discuss specific issues (e.g., a proposed study design, alternative approach or additional study expectations) or questions, in which FDA will provide targeted advice regarding an ongoing ANDA development program.

X. **Review Status Update** – means a response from the regulatory project manager (RPM) to the Authorized Representative to update the Authorized Representative concerning, at a minimum, the categorical status of relevant review disciplines with respect to the submission at that time. A review status update is preliminary only based on the RPM's interpretation of the submission and subject to change at any time.

Y. **Standard controlled correspondence (CC)** – means controlled correspondence:

1. As described in CDER's September 2015 guidance for industry *Controlled Correspondence Related to Generic Drug Development* or

2. Concerning post-approval submission requirements that are not covered by CDER's post-approval changes guidance and are not specific to an ANDA.

Z. **Refuse to Receive (RTR)** means refusal to receive an ANDA for review. See 21 CFR 314.101 and the guidance for industry *ANDA Submissions – Refuse-to-Receive Standards* (December 2016). See https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

AA. **Submission** refers to an ANDA, an amendment to an ANDA, a PAS to an ANDA, or an amendment to a PAS.

BB. **Submission date** means the date that a generic drug submission or Type II DMF is deemed to be "submitted" pursuant to Section 744B(a)(6) of the FD&C Act, which states that a generic drug submission or Type II DMF is deemed to be "submitted" if it is submitted via an FDA electronic gateway, on the day when transmission to that electronic gateway is completed, except that, when the submission or DMF arrives on a weekend, Federal holiday, or day when the FDA office that will review that submission is not otherwise open for business, the submission shall be deemed to be submitted on the next day when that office is open for business. In section 745A(a) of the FD&C Act, Congress granted explicit authorization to FDA to implement the statutory electronic submission requirements in guidance. Refer to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (January 2019). See https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

CC. **Tentative Approval (TA) Letter** - If a generic drug product is ready for approval but cannot be approved because of a patent or exclusivity related to the RLD product, FDA issues a TA letter to the applicant, and the TA letter details the basis for the TA. FDA will not issue final approval of the generic drug product until all patent or exclusivity issues

have been resolved or, in some cases, until a 30-month stay associated with patent litigation has expired. A TA does not allow the applicant to market the generic drug product.

DD. **Type II API Drug Master File (DMF)** - A submission of information to FDA concerning the manufacture of a pharmaceutical active ingredient by a person that intends to authorize FDA to reference the information to support approval of a generic drug submission without the submitter having to disclose the information to the generic drug submission applicant.

Appendix B: FY 2020 GDUFA Science and Research Priority Initiatives

Under GDUFA, FDA committed to developing an annual list of regulatory science and research priority initiatives for generic drugs. The priority initiatives are organized according to the categories of complex generic drug products described in the GDUFA II Commitment Letter, followed by a category addressing topics related to tools and methodologies for evaluating BE and therapeutic equivalence more generally. These initiatives are based on the need to develop efficient and modern generic drug research, development, and review tools:

A - Complex active ingredients, formulations, or dosage forms

1. Improve advanced analytics for characterization of chemical compositions, molecular structures, and distributions in complex active ingredients.
2. Improve particle size, shape, and surface characterization to support a demonstration of therapeutic equivalence of suspended and colloidal drug products.
3. Establish predictive in silico, in vitro, and animal models to evaluate the immunogenicity risk of formulation or impurity differences in generic products.
4. Develop predictive in vitro BE methods for long-acting injectable drug products including the identification of the critical quality attributes for these products.
5. Develop better methods for evaluating abuse deterrence of generic, solid, oral opioid products, including in vitro alternatives to in vivo nasal studies.

B - Complex routes of delivery

1. Improve physiologically based PBPK models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic).
2. Expand characterization-based BE methods across all topical dermatological products.
3. Expand characterization-based BE methods across all non-solution ophthalmic products.
4. Develop more efficient alternatives to the use of forced expiratory volume in one second comparative clinical endpoint BE studies for inhaled corticosteroids.
5. Develop alternatives to comparative clinical endpoint BE studies for locally-acting nasal products that are more predictive of and sensitive to differences in local delivery.

C - Complex drug-device combinations

1. Evaluate the impact of identified differences in the user-interface from the rRLD on the therapeutic equivalence of complex generic drug-device combination products.
2. Develop criteria for device performance comparisons that would support a BE demonstration by in vitro methods and eliminate the need for in vivo BE.

D - Tools and methodologies for BE and therapeutic equivalence evaluation

1. Improve quantitative pharmacology and BE trial simulation to optimize design of BE studies for complex generic drug products.
2. Integrate predictive dissolution, PBPK, and pharmacokinetic/pharmacodynamic models establishing generic drug BE standards.
3. Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System of Class 3 biowaivers to drug products with differences in formulations larger than currently recommended in FDA guidance.

4. Develop methods and integrated technological solutions that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution/utilization patterns, drug safety data, and drug quality data) to support regulatory decisions and improve post-market surveillance of generic drug substitution.

Appendix C: Analysis of Use of Funds

On August 18, 2017, FDARA (Public Law 115-52) was signed into law. FDARA amends the FD&C Act to revise and extend the user fee programs for human drugs, biologics, generic drugs, medical devices, and biosimilar biological products.

FDARA requires specified analyses of the use of funds in the annual performance reports of each of the human medical product user fee programs. The analyses include information such as differences between aggregate numbers of submissions and certain decisions, an analysis of performance goals, a determination of causes affecting the ability to meet goals, and the issuance of corrective action reports.

Section 904(c)(1) of FDARA requires that the analysis of use of funds include information on (1) the difference between aggregate numbers of ANDAs filed and certain types of decisions, (2) an analysis of performance enhancement goals, and (3) a determination of causes affecting the ability to meet goals.

A. Aggregate Number of ANDAs Received and Certain Types of Decisions

Although the mandate is to report the number of ANDAs *filed*, the term "received" is used instead of "filed" in the statute with respect to ANDAs. FDA will thus report on the aggregate number of ANDAs *received*. Per 21 CFR 314.101(b)(1), an ANDA will be reviewed after it is submitted to determine whether the ANDA can be "received." "Receipt of an ANDA" means that FDA made a threshold determination that the ANDA is substantially complete. A "substantially complete ANDA" is an ANDA that on its face is sufficiently complete to permit a substantive review. "Sufficiently complete" means that the ANDA contains all the information required under section 505(j)(2)(A) of the FD&C Act and does not contain a deficiency described in 21 CFR 314.101(d) and (e). The number of ANDAs *received* in the table below does not account for submissions that were determined to not be substantially complete.

Goal Type FY 2018 Final Performance	Review Goal	Received	Received with Goal Post FY 2018	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
I. Original ANDA Review Goals									
Standard Original ANDA Applications	10 months	556	523	104	20	408	24	96%	93% to 96%
Priority Original ANDA Applications (if applicant meets requirements of a PFC)	8 months	28	25	4	0	24	0	100%	100% to 100%
Priority Original ANDA Applications (if applicant does not meet the requirements of a PFC)	10 months	377	311	24	9	339	12	97%	96% to 97%
II. Amendment Review Goals									
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	751	544	167	23	547	29	96%	95% to 96%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	37	37	9	2	24	0	100%	95% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	284	205	47	26	208	15	95%	95% to 95%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	1	1	0	0	1	0	100%	100% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	10	10	2	0	8	0	100%	100% to 100%

Goal Type FY 2018 Final Performance	Review Goal	Received	Received with Goal Post FY 2018	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
Standard and Priority Minor ANDA Amendments	3 months	1,246	430	487	159	596	107	91%	91% to 91%

*Missed Goals include submissions that have not had an action and have passed the goal date.

†These percentages include Refuse to Receive actions, Withdrawn submissions, and Pending submissions, in addition to Approval, TA, and CR actions.

Goal Type FY 2019 Preliminary Performance	Review Goal	Received	Received with Goal post FY 2019	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
I. Original ANDA Review Goals									
Standard Original ANDA Applications	10 months	523	455	10	0	66	3	97%	20% to 99%
Priority Original ANDA Applications (if applicant meets requirements of a PFC)	8 months	37	20	5	0	13	0	100%	49% to 100%
Priority Original ANDA Applications (if applicant does not meet the requirements of a PFC)	10 months	235	197	0	1	40	0	100%	21% to 100%
II. Amendment Review Goals									
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	846	592	30	7	228	6	98%	32% to 99%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	38	22	0	1	15	0	100%	42% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	286	128	24	3	138	8	95%	57% to 97%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	3	2	0	1	0	0	100%	33% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	16	11	1	0	4	0	100%	31% to 100%
Standard and Priority Minor ANDA Amendments	3 months	1,079	294	340	84	380	64	92%	69% to 94%

*Missed Goals include submissions that have not had an action and have passed the goal date.

†These percentages include Refuse to Receive actions, Withdrawn submissions, and Pending submissions, in addition to Approval, TA, and CR actions.

B. Performance Enhancement Goals Met

The following table addresses section 904(c)(1) of FDARA, pertaining to GDUFA, which requires FDA to include relevant data to determine whether CDER and CBER have met performance enhancement goals identified in the letters described in section 301(b) of GDUFA II (GDUFA II Commitment Letter) for the applicable fiscal year.

For the purposes of this report, “performance enhancement goals” are defined as any non-review goal described in the GDUFA II Commitment Letter with a specified goal date that falls within the applicable fiscal year.

Performance Enhancement Goal	Target Goal Date	On Time (Y/N)	Actual Completion Date	Comments
Update the Inactive Ingredient Database on an ongoing basis and post quarterly notice of updates made.	Quarterly	Y	Quarterly	https://www.fda.gov/drugs/drug-approvals-and-databases/most-recent-changes-iid-database
Conduct a public workshop to solicit input from industry and stakeholders for inclusion in an annual list of GDUFA II Regulatory Science initiatives.	Annually	Y	Public Workshop Held May 1, 2019	https://www.fda.gov/news-events/fy-2019-generic-drug-regulatory-science-initiatives-public-workshop-05012019-05012019
Hold meetings between FDA and industry GDUFA II regulatory science working group.	Biannually	Y	First Meeting Held February 25, 2019. Second Meeting Held on September 17, 2019	https://www.fda.gov/drugs/generic-drugs/generic-drugs-priorities-projects
Issue a guidance regarding post-approval changes to a Type II API DMF	10/1/2018	Y	9/11/2018	https://www.fda.gov/media/115733/download
Publish monthly reporting metrics set forth under section VI(C)(1)(a) through (d) of the GDUFA II Commitment Letter	Monthly	Y	Monthly	FDA posted these monthly metrics at https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/activities-report-generic-drugs-program-fy-2019-monthly-performance
Publish quarterly reporting metrics set forth under section VI(C)(2)(a) through (d) of the GDUFA II Commitment Letter	Quarterly	Y	Quarterly	FDA posted these quarterly metrics at https://www.fda.gov/industry/activities-report-generic-drugs-program-fy-2019-gdufa-ii-quarterly-performance
Publish annual reporting metrics set forth under section VI(C)(3)(a) through (p) of the GDUFA II Commitment Letter	Annual	Y	Annual	Please see the Performance Reporting Section of the FY 2019 GDUFA Performance Report.
Publish updates to the GDUFA Five-Year Financial Plan no later than the 2nd quarter of each subsequent fiscal year	3/31/2019	N	5/31/2019	FDA published the FY 2019 GDUFA Five-Year Financial Plan update in May 2019 because of the federal government shutdown

Performance Enhancement Goal	Target Goal Date	On Time (Y/N)	Actual Completion Date	Comments
Convene a public meeting no later than the third quarter of each fiscal year starting in FY 2019 to discuss the GDUFA Five-Year Financial Plan, along with the Agency's progress in implementing modernized time reporting and resource management planning	6/30/2019	Y	6/7/2019	FDA held the public meeting to discuss the GDUFA Five-Year Financial Plan in June 2019

C. Common Causes and Trends Impacting Ability to Meet Goals

This section addresses section 904(c)(1) of FDARA, pertaining to GDUFA II, which requires FDA to identify the most common causes and trends for external or other circumstances affecting the ability of FDA to meet the review time and performance enhancement goals identified in the GDUFA II Commitment Letter.

The table below represents FDA's FY 2018 updated performance.

Cause or Trend	Impact on FDA's Ability to Meet Goals
Small number of submissions for the Priority PAS (if pre-approval inspection is required and applicant does not meet the requirement of a PFC) and Priority Major PAS (if pre-approval inspection is not required) review goals	In last year's report, the Agency could not fully report on this in this appendix because some of the submissions that fell under this review goal category had review time goals that fell within FY 2019. As stated in last year's report, the Agency can now fulfill the commitment to fully report its performance on review goals. Both review goals had very small cohorts, which create challenges in meeting the 90% metric when a single review goal is missed.

The table below represents FDA's FY 2019 preliminary performance.

Cause or Trend	Impact FDA Ability to Meet Goals
Short time to receive a scheduled date for a requested Post-CRL teleconference within 10 calendar days of the request for a teleconference	The 10-calendar-day goal includes weekends and holidays. The request must be electronically received by one part of the Agency and sent to another part of the Agency for triaging before the Agency can determine if the meeting request should be granted. If it is granted, the RPM must schedule the meeting and communicate the meeting date back to the applicant. Although these steps are not complicated, they are numerous, and the Agency faces challenges with meeting some of these goals, especially when weekends and holidays are included within the goal.
Small number of submissions for FDA to issue safety determination letters within 60 calendar days of the date of submission of disclosure authorization	The Agency missed issuing one out of three safety determination letters within 60 calendar days of submission of the disclosure authorization. The Agency remains steadfast in striving to issue each letter within the established timeframe.
Federal government shutdown	The federal government shutdown resulted in the late publication of the FY19 update to the GDUFA Five-Year Financial Plan.

Appendix D: FY 2019 Corrective Action Report

FY 2019 Corrective Action Report

On August 18, 2017, FDARA (Public Law 115-52) was signed into law. FDARA amends the FD&C Act to revise and extend the user fee programs for human drugs, biologics, medical devices, and biosimilar biological products, and for other purposes. Among the provisions of Title IX, section 904 of FDARA, FDA is required to issue a corrective action report that details FDA's performance in meeting the review and performance enhancement goals identified in the letter described in section 301(b) of GDUFA II (i.e., the GDUFA II Commitment Letter) for the applicable fiscal year.

If the Secretary determines, based on the analysis presented in the GDUFA Annual Performance Report, that each of the review and performance enhancement goals for the applicable fiscal year have been met, the corrective action report shall include recommendations on ways in which the Secretary can improve and streamline the human drug application process.[46]

For any of the review and performance enhancement goals during the applicable fiscal year that were not met, the corrective action report shall include a justification, as applicable, for the types of circumstances and trends that contributed to missed review goal times; and with respect to performance enhancement goals that were not met, a description of the efforts FDA has put in place to improve the ability of the Agency to meet each goal in the coming fiscal year. Such a description of corrective efforts is not required by statute for review time goals, but FDA is nonetheless providing this information in an effort to be complete.

This report satisfies this reporting requirement.

[46] Section 744C(c)(1) of the FD&C Act (21 U.S.C. 379j-43(c)(1)).

Executive Summary

FY 2018 Review Goal Performance

The following table represents FDA's FY 2018 updated performance for goal types that the Agency was not able to fully report in last year's report. If a goal type is not listed in this table for FY 2018, then the Agency fully reported on it in last year's report.[47]

Goal Type	Circumstances and Trends Impacting Ability to Meet Goal Date	Corrective Action Plan
Review Goals	Because of the small number of submissions for the Priority PAS (if pre-approval inspection is required and applicant does not meet the requirement of a PFC) and Priority Major PAS (if pre-approval inspection is not required) review goals, missing the goal of a single submission resulted in dropping below the 90% GDUFA metric.	FDA is committed to meeting its goals and continues to strive to meet every goal in these cohorts in the coming years.
Review Program Enhancement Goals	All FY 2018 goals were met.	No corrective action plan is needed.
Pre-ANDA Program Goals	All FY 2018 goals were met.	No corrective action plan is needed.
Facilities Goals	All but one facility goal were met. Upon receipt of a written or email request by an establishment physically located in the United States that has been included as part of a marketing application submitted to a foreign regulator, FDA will 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. FDA did not meet this goal.	FDA is committed to meeting its goals and continues to strive to meet them in the next year as it continues to implement this program. FDA notes that the inspection classifications database meets a GDUFA II commitment regarding communications with foreign regulators. The database also facilitates foreign regulators' ability to independently check the most recent inspection classification.

[47] https://www.fda.gov/about-fda/user-fee-performance-reports/gdufa-performance-reports

The following table represents FDA's FY 2019 preliminary performance.

Goal Type	Circumstances and Trends Impacting Ability to Meet Goal Date	Corrective Action Plan
Review Goals	Too soon to determine.	Some submissions received in FY 2019 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot yet evaluate the entire performance for FY 2019 review time goals, FDA will provide a full evaluation next year.
Review Program Enhancement Goals	All FY 2019 goals were met.	No corrective action plan is needed.
Pre-ANDA Program Goals	Too soon to determine.	Some submissions received in FY 2019 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot yet evaluate the entire performance for FY 2019 review time goals, FDA will provide a full evaluation next year.
Facilities Goals	All but one facility goal were met. Upon receipt of a written or email request by an establishment physically located in the United States that has been included as part of a marketing application submitted to a foreign regulator, FDA will 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. FDA accomplished this goal by 45%. FDA received 9 such requests in FY19 and replied to 5 outside of the 30-day timeframe.	FDA is committed to meeting its goals and continues to strive to meet them in the next year as we continue to implement this program. FDA notes that the inspection classifications database meets a GDUFA II commitment regarding communications with foreign regulators. The database also facilitates foreign regulators' ability to independently check the most recent inspection classification.
Enhanced Accountability and Reporting Goals	All FY 2019 goals were met.	No corrective action plan is needed.
Policy Documents	All FY 2019 goals were met.	No corrective action plan is needed.
Public Meetings and Workshops	All FY 2019 goals were met.	No corrective action plan is needed.
Program and Process Implementation	All FY 2019 goals were met.	No corrective action plan is needed.
Reporting	FDA published the FY 2019 GDUFA Five-Year Financial Plan update in May 2019, due to the federal government shutdown.	Barring another government shutdown, there should be no delay in publishing the FY20 GDUFA Five-Year Financial Plan.
Website Publishing	All FY 2019 goals were met.	No corrective action plan is needed.

GDUFA Review Goals

The following section addresses section 904(c)(2)(B) of FDARA (section 744C(c)(2)(A) of the FD&C Act), which requires the FDA to provide a justification for the determination of review goals missed during FYs 2018 and 2019 and a description of the circumstances and any trends related to missed review goals.

This section presents GDUFA performance and workload information for all review performance goals for ANDAs.

I. FY 2018 Review Goal Performance

A. Summary of Performance: *A small number of submissions for the Priority PAS (if pre-approval inspection is required and applicant does not meet the requirement of a PFC) and Priority Major PAS (if pre-approval inspection is not required) review goals was missed during FY 2018.*

B. Justification: *Because of to a very small number of submissions, missing the goal for a single submission resulted in dropping below the GDUFA metric of 90 percent.*

C. FY 2019 Corrective Actions: *FDA will continue to strive to meet all GDUFA review goal dates.*

II. FY 2019 Review Goal Performance

A. ***Summary of Performance:*** *The Agency is aware that it has missed some review goals, but because some submissions received in FY 2019 having associated review goals that fall within the subsequent fiscal year, FDA cannot yet evaluate the entire performance for FY 2019 review time goals. FDA will provide a full evaluation next year.*

B. ***Justification:*** *Too soon to determine the justification.*

C. FY 2020 Corrective Actions: *Too soon to determine the corrective action, but FDA is committed to pursuing corrective actions as needed.*

III. FY 2019 Pre-ANDA Goals Performance

A. ***Summary of Performance:*** *Some submissions received in FY 2019 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot yet evaluate the entire performance for FY 2019 review time goals, FDA will provide a full evaluation next year.*

B. ***Justification:*** *Too soon to determine if a justification is needed.*

C. ***FY 2020 Corrective Actions:*** *Too soon to determine if a corrective action is needed.*

IV. FY 2019 Facilities Goals Performance

A. ***Summary of Performance:*** *The Agency has partially missed one of the facilities goals. Under the GDUFA II Commitment Letter, upon receipt of a written or email request by an establishment physically located in the United States that has been included as part of a marketing application submitted to a foreign regulator, FDA will 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. FDA is committed to accomplishing this goal in the next year. FDA notes that under GDUFA II, FDA committed to updating the inspection classifications database by January 1, 2019, and to continue to update it every 30 days. Because of the interest in making this information available to drug manufacturers, applicants, foreign regulators, and the public, FDA worked diligently to complete the commitment in advance of that goal. Moreover, FDA's Office of Regulatory Affairs worked with the Agency's product centers to go beyond the commitment by including available information and updating the database every 30 days for inspections of all FDA-regulated medical products.*

B. ***Justification:*** *FDA is actively pursuing additional resources for this program. However, CGMP declarations are only one of several ways that FDA is enhancing communication and transparency with foreign regulatory authorities regarding the compliance status of establishments in the United States. Foreign regulators can also find the CGMP status of an establishment by checking the inspection classifications database for the most recent inspection classification.*

C. ***FY 2020 Corrective Actions:*** *FDA is actively pursuing additional resources for this program.*

V. FY 2019 Enhanced Accountability and Reporting Goals Performance

A. ***Summary of Performance:*** *All FY 2019 goals were met.*

B. ***Justification:*** *No justification is needed.*

C. ***FY 2020 Corrective Actions:*** *No corrective action is needed.*

VI. FY 2019 Website Publishing

A. ***Summary of Performance:*** *All FY 2019 goals were met.*

B. ***Justification:*** *No justification is needed.*

C. ***FY 2020 Corrective Actions:*** *No corrective action is needed.*

VII. Reporting

A. ***Summary of Performance:*** FDA missed the GDUFA goal for publishing an update to the GDUFA Five-Year Financial Plan.

B. ***Justification:*** FDA published the FY 2019 GDUFA Five-Year Financial Plan Update in May 2019 because of the federal government shutdown.

C. ***FY 2020 Corrective Actions:*** Assuming there is no government shutdown in 2020, there should not be a delay in publishing the FY 2020 GDUFA Five-Year Financial Plan. In addition, FDA has concurrently been working to streamline internal processes to speed publishing and mitigate risk of missing the timelines regardless of external factors (e.g., a government shutdown).

GDUFA Performance Enhancement Goals

The following section addresses section 904(c)(2) of FDARA (section 744C(c)(2) of the FD&C Act), which requires FDA to provide a detailed description of the efforts its has put in place for the fiscal year in which the report is submitted to improve FDA's ability to meet performance enhancement goals during FY 2020.

This section presents non-review performance goals cited in the GDUFA II Commitment Letter with required completion dates in FY 2019. For the purposes of this report, "performance enhancement goals" are defined as any non-review performance goal with a specified deadline as named in the GDUFA II Commitment Letter. Performance enhancement goals with specified completion dates in FY 2020 through FY 2022 will be covered in subsequent corrective action reports.

FDA was able to meet all its non-review performance goals with specified deadlines in the GDUFA II Commitment Letter and therefore, no description of efforts to meet those goals in FY 2020 is necessary.

Department of Health and Human Services
Food and Drug Administration

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Office of Planning
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002
Phone: 301-796-4850

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