FY 2021

PERFORMANCE REPORT
TO
CONGRESS

for the

Generic Drug User Fee Amendments

(This page left blank intentionally.)

Commissioner's Report

I am pleased to present to Congress the Food and Drug Administration's (FDA's or Agency's) fiscal year (FY) 2021 performance report on the Generic Drug User Fee Amendments (GDUFA) program. This report details FDA's preliminary accomplishments in FY 2021 (October 1, 2020, through September 30, 2021) and updates FDA's performance results for the previous fiscal year of GDUFA. This report covers the fourth year of the GDUFA reauthorization of 2017, also referred to as "GDUFA II."

With the reauthorization of the GDUFA program in 2017, FDA acquired additional performance goals and higher expectations for program enhancements and approvals. Subsequently, the Agency has implemented quality systems to improve the efficiency of the review process. FDA continues to employ innovative processes to ensure the approval of safe and effective generic products.

I am confident that the new processes introduced through GDUFA II and activities taken under FDA's Drug Competition Action Plan[1] will continue to help reduce review cycles, improve approval times, and 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, especially with the unforeseen challenges and obstacles due to the COVID-19 pandemic. Despite the challenges of transitioning to a remote work environment, and with an increased workload due to the expedited development and review of generic drug products to help address the COVID-19 public health emergency, FDA rose to the challenge and maintained its high level of performance in meeting GDUFA's goals and initiatives.

I look forward to continued engagement with the generic drug industry, Congress, and other stakeholders.

Janet Woodcock, M.D.
Acting Commissioner of Food and Drugs

[1] www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan.

Acronyms

ANDA – Abbreviated New Drug Application

AI – Artificial Intelligence

API – Active Pharmaceutical Ingredient

APSD – Aerodynamic Particle Size Distribution

BE – Bioequivalence

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

CFD – Computational Fluid Dynamics

DMF – Drug Master File

DRL – Discipline Review Letter

eCTD – Electronic Common Technical Document

EU – European Union

FDA – Food and Drug Administration

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

FDARA – FDA Reauthorization Act of 2017

FDF – Finished Dosage Form

FTE – Full-Time Equivalent

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

IVRT – In Vitro Release Test

MAPP – Manual of Policies and Procedures

MRA – Mutual Recognition Agreement

NAI – No Action Indicated

OAI – Official Action Indicated

OC – Office of the Commissioner

ORA – Office of Regulatory Affairs

PAI – Pre-Approval Inspection

PAS – Prior Approval Supplement

PBPK – Physiologically Based Pharmacokinetic

PD – Pharmacodynamic

PFC – Pre-Submission Facility Correspondence

PK – Pharmacokinetic

PSG – Product-Specific Guidance

RLD – Reference Listed Drug

RPM – Regulatory Project Manager

RTR – Refuse to Receive

SBIA – Small Business & Industry Assistance

TA – Tentative Approval

USP – United States Pharmacopeia

UL – Untitled Letter

VAI – Voluntary Action Indicated

WL – Warning Letter

WCF – Working Capital Fund

(This page left blank intentionally.)

Executive Summary

On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act,[2] 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 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),[3] 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: (1) reducing the number of review cycles to approval and (2) increasing the number of approvals of safe, effective, high-quality, and lower-cost generic drugs.

This collaborative work included identifying opportunities for earlier and enhanced communications to support the efficient and effective pre-market review of generic drugs. This communication has been 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 introduced in GDUFA II is the pre-abbreviated new drug application (pre-ANDA) program, which has strengthened and diversified the pipeline of generic drug applications with a robust development pathway that includes support to developers of complex generic drug products. The pre-ANDA program features Product Development, Pre-Submission, and Mid-Review Cycle meetings that provide clarity around regulatory expectations for prospective applicants early in the generic product development cycle and assist with the development of more complete application submissions, with the ultimate goal of reducing a generic product's time in the pipeline from concept, to development, to market.

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, the American people. This annual report presents preliminary data on FDA's success in meeting fiscal year (FY) 2021 review goals and commitments for GDUFA II and updates the data for FY 2020.

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

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

Highlighted Achievements – FY 2021

In FY 2021, FDA experienced the continued impact of the COVID-19 public health emergency. The COVID-19 pandemic resulted in a shift to 100 percent virtual work for the majority of Agency staff. The Agency appropriately shifted resources to prioritize work focused on addressing the pandemic. Despite this, FDA managed to meet the FY 2021 review performance goals. Highlights of these activities are provided below.

Generic Drug Assessment and Approval Activity Highlights:

In FY 2021, FDA approved 679 abbreviated new drug applications (ANDAs)[4] and tentatively approved[5] 157 ANDAs.

A critically important subset of these generic drug approvals is the category of first generics. First generics provide access to needed therapies that treat a wide range of medical conditions and for which no generic competition has previously existed. First generic approvals are particularly important to public health, and FDA prioritizes the review of first generic submissions.

Significant first generic approvals for FY 2021 include glucagon for injection packaged in an emergency kit (the reference listed drug (RLD)[6] is Glucagon), linaclotide capsules (the RLD is Linzess), difluprednate ophthalmic emulsion (the RLD is Durezol), and apremilast tablets (the RLD is Otezla). A list of all first-time generic approvals for each calendar year is posted on FDA's first generic drug approvals website.[7]

FDA also is increasing the number of approvals of products for which there is insufficient generic drug competition under the competitive generic therapy (CGT) process established in FDARA. In this process, FDA designates and expedites the development and review of ANDAs for drug products that meet the *CGT* definition. In January 2020, to provide transparency on these designations, FDA created a web page listing all CGT approvals,[8] including exclusivity eligibility, and the corresponding dates of marketing and/or forfeiture of exclusivity.

In FY 2021, 37 generic drug products (which were the subjects of 24 ANDAs) were approved with CGT exclusivity, with an average time to market after approval of around 29 days for these products. The successful implementation of the CGT pathway demonstrates that it is efficient and effective at promoting competition from new generic drug products. During FY 2021, FDA

---

[4] The definition of an *ANDA* can be found in Appendix A of the report.

[5] *Tentative approval* is a notification to an ANDA applicant that the ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act but cannot be approved because of unexpired patents or exclusivities. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval letter after any necessary additional review of the ANDA.

[6] The definition of an *RLD* can be found in Appendix A of the report.

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

[8] www.fda.gov/drugs/generic-drugs/competitive-generic-therapy-approvals.

updated the CGT web page every 2 weeks to continue its transparency efforts for this important program.

Further, in FY 2021, despite the challenges of prioritizing COVID-19-related work, FDA met key performance goals and approved more than 37 original ANDAs and more than 533 supplements for products related to COVID-19.

Pre-ANDA Program Highlights:

GDUFA II's pre-ANDA program is showing strong signs of success. For example, during FY 2021, FDA facilitated 87 product development and pre-submission pre-ANDA meetings for prospective applicants, published 53 product-specific guidances (PSGs) for complex products, and addressed 259 controlled correspondence (CC) for complex products. Pre-ANDA program information is posted on FDA's pre-ANDA program and complex generic products website.[9] Additional details on this important program are provided below in this report.

Review Efficiency Highlights:

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

- 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, 2021, FDA has met 99 percent of the FY 2021 goals for these applications.

- FDA agreed to review and act on priority original ANDA submissions with an 8-month goal date if the applicant submits a Pre-Submission Facility Correspondence (PFC) 2 months prior to the date of ANDA submission and the PFC is found to be complete and accurate and remains unchanged. As of September 30, 2021, FDA has met 100 percent of the FY 2021 goals for these applications.

- FDA agreed to review and act on standard prior approval supplements (PASs) within 6 months of the date of submission if no inspection is needed (i.e., a 6-month goal date). As of September 30, 2021, FDA has met 98 percent of the FY 2021 goals for these applications.

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 agreed in GDUFA II to issue communications related to preliminary thoughts on possible ANDA deficiencies (i.e., discipline review letters (DRLs)) and requests for further information or clarifications during the course of the review of original ANDAs. FDA continues to embrace these mechanisms and communicate extensively with industry. As of September 30, 2021, FDA issued 4,313 information

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

requests and 2,230 DRLs. These requests and letters detail important issues that need to be addressed by applicants before FDA can act on an application. These and other important activities are posted on FDA's Generic Drugs Program Activities Report (FY 2021) Monthly Performance website.[10]

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 3,897 CCs during FY 2021, a number that has more than quadrupled since the beginning of GDUFA I. Even with the substantial increase, as of September 30, 2021, FDA continues to exceed the GDUFA II goals with a 98 percent timely response rate for all standard CC and a 95 percent timely response rate for all complex CC.

FDA's efforts to increase review efficiency and thereby improve patient access to generic drugs also have been greatly enhanced by the Agency's publication of guidances for industry on 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.

Timely recommendations from the Agency allow generic drug applicants to build those recommendations into their research and development programs, which helps them submit higher quality ANDAs. There are a variety of ways FDA makes its regulatory and scientific policies available to applicants and the general public, including:

- Regulatory guidances for industry - These are available through FDA's Guidance Documents database website.[11]

- Manuals of Policies and Procedures (MAPPs) – These describe internal Agency policies and procedures and are accessible to the public to help make the Agency's operations more transparent. MAPPs are available on FDA's MAPP website.[12]

In FY 2021, FDA issued various policy documents, including several guidances for industry (not including PSGs), *Federal Register* notices, and MAPPs. In addition to these general guidances for industry and other policy-related resources, FDA provided important scientific guidance and recommendations to give generic drug applicants better opportunities to efficiently develop generic drug products and to prepare more complete ANDAs. These recommendations are often

[10] www.fda.gov/drugs/abbreviated-new-drug-application-anda/activities-report-generic-drugs-program-fy-2020-monthly-performance.

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

[12] www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp.

described in PSGs.[13] FDA developed these-recommendations based on public health priorities, requests from industry, then-current and anticipated patient and industry needs, and scientific research.

In FY 2021, FDA issued 135 PSGs (53 for complex products). As of September 30, 2021, FDA had published approximately 1,921 PSGs on FDA's Product-Specific Guidances for Generic Drug Development website.[14]

In addition to issuing regulatory guidances for industry, MAPPs, and PSGs, in FY 2021, FDA engaged in other efforts to increase its transparency and enhance communications for generic drug developers. For example, October 31, 2020, marked the 40th anniversary of the first official publication of *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the Orange Book. Coinciding with this milestone, FDA has been actively considering ways to make this key resource as useful as possible for stakeholders, including any improvements that could be made to advance the Agency's goal of improving access to high-quality, more affordable treatment options for Americans. In addition, on January 5, 2021, the Orange Book Transparency Act of 2020 (Pub. L. 116-290) was signed into law. Consistent with this new law, FDA solicited public comment regarding the types of patent information that should be included in, or removed from, the Orange Book and will transmit to Congress, by January 5, 2022, a summary of the comments received and the actions the Agency is considering taking, if any, in response to these comments.

In addition, in FY 2021, FDA continued implementation of the law widely known as "CREATES,"[15] which was enacted in December 2019 as part of the Further Consolidated Appropriations Act, 2020 (Pub. L. 116-94). CREATES made available an important new pathway for developers of potential drug and biological products to obtain samples of brand products that they need to support their applications. In FY 2021, FDA issued 23 Covered Product Authorizations (CPAs) to generic product developers seeking to obtain samples of brand products that are subject to a Risk Evaluation and Mitigation Strategy with elements to assure safe use. All CPAs were issued within the 120-day timeline mandated by CREATES; the successful implementation of this new authority has allowed generic product developers to more easily obtain the samples needed for product development and testing and, ultimately, for the submission of ANDAs.

---

[13] PSGs provide the Agency's current thinking and expectations on how to develop generic drugs that are therapeutically equivalent to specific brand-name RLDs. PSGs are intended to help make industry's research and development decisions more efficient and cost effective by identifying the most appropriate methodology and evidence needed to support a specific generic drug's approval. PSGs also help applicants submit ANDAs with fewer deficiencies, which can lead to more first-cycle approvals.

[14] www.fda.gov/drugs/guidances-drugs/product-specific-guidances-generic-drug-development.

[15] The "CREATES Act" was the short title of a 116th Congress bill, the "Creating and Restoring Equal Access To Equivalent Samples Act." The enacted law is section 610, *Actions for Delays of Generic Drugs and Biosimilar Biological Products*, of Division N of Pub. L. 116-94, the Further Consolidated Appropriations Act, 2020.

GDUFA Science and Research Program Highlights:

The GDUFA Science and Research Program is an integral part of the Agency's GDUFA commitments. The program helps advance the science of generic drugs by investigating scientific issues that are encountered during the review of regulatory submissions.

FDA consults with and solicits input from the public, industry, and academia to develop an annual list of the GDUFA regulatory science initiatives specific to research on generic drugs. In FY 2021, FDA awarded 6 new research contracts and 10 new grants[16] for innovative research projects on generic drugs. FDA also utilized its laboratories, personnel, and computer systems to conduct more than 80 GDUFA Science and Research projects. Each fiscal year, FDA provides details on these projects in its annual GDUFA Science and Research Report.[17] The FY 2021 GDUFA Science and Research Report provides detailed results for 13 areas of focus, including research activities and comprehensive lists of grants and contracts that the GDUFA Science and Research Program awarded in FY 2021.

Ongoing scientific research under GDUFA[18] has enabled FDA to make recommendations that support appropriate science-based methodologies and evidence for the development of many generic drugs, including complex generics. The FDA-supported GDUFA Science and Research Program generated more than 70 peer-reviewed scholarly articles, one provisional patent, more than 100 external talks, and more than 75 posters that were exhibited at national and international scientific and medical conferences related to generic drugs. See the discussion of "Significant FY 2021 GDUFA Science and Research Accomplishments" in Appendix B of the report.

Regulatory and Scientific Outreach Activities Highlights:

FDA's GDUFA Science and Research Report web page[19] lists all research outcomes for the previous fiscal year in one easily accessible place. This web page provides greater public transparency regarding the important work the generic drug program engages in to advance the science of generic drugs. Information about this work is provided to generic drug developers, applicants, and assessors, along with essential tools and information to help expedite the availability of safe, effective, and high-quality generic drugs. In addition, the web page provides information on the GDUFA research outcomes supporting the following:

1. The development of generic drug products,

2. The generation of evidence needed to support the efficient review and timely approval of ANDAs, and

[16] www.fda.gov/drugs/generic-drugs/generic-drug-research-priorities-projects.

[17] www.fda.gov/drugs/generic-drugs/generic-drug-research-related-guidances-reports.

[18] www.fda.gov/drugs/generic-drugs/generic-drug-research-priorities-projects.

[19] www.fda.gov/drugs/generic-drugs/generic-drug-research-related-guidances-reports.

3. The evaluation of generic drug equivalence throughout a given fiscal year.

The FY 2022 generic drug regulatory science priority initiatives that have been identified are grouped into the following 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 bioequivalence (BE) and therapeutic equivalence evaluations

In FY 2021, FDA engaged in significant outreach efforts to educate and inform industry participants and other stakeholders about GDUFA II and the generic drugs program. For example, FDA supported the development of the newly formed Center for Research on Complex Generics (CRCG)[20] through multiple activities to reach out to external stakeholders including the generic drug industry. The CRCG, in addition to ensuring that GDUFA research initiatives are focused on the most pressing scientific challenges, is committed to helping generic industry stakeholders efficiently access and effectively utilize the scientific insights, technical methods, study designs, data analyses, and other GDUFA Science and Research Program outcomes to successfully develop complex generics. During FY 2021, the CRCG solicited and received feedback from a wide range of generic industry stakeholders that not only provided more detailed insights into specific challenges related to the development and assessment of complex generics but also helped identify actionable outcomes that can address these challenges.

Also in FY 2021, FDA hosted or co-hosted several meetings, webinars, and public workshops, including the following:

The FDA/DIA Complex Generic Drug-Device Combination Products Conference 2020 www.fda.gov/drugs/news-events-human-drugs/fdadia-complex-generic-drug-device-combination-products-conference-2020-10192020-10202020 This workshop examined both the current state of knowledge about complex drug-device combination products and FDA's ongoing scientific research supporting the evidence-based development, assessment, and approval of complex generic drug-device combination products. Speakers discussed these topics, as well as common issues that may arise during	October 19-20, 2020

[20] www.complexgenerics.org/.

the assessment of ANDAs, general expectations for industry after product approval, and future directions.	
FDA's Small Business & Industry Assistance (SBIA) Regulatory Education for Industry (REdI) Conference: Celebrating 40 Years: An In-Depth Examination of the FDA Orange Book www.fda.gov/drugs/news-events-human-drugs/regulatory-education-industry-celebrating-40-years-depth-examination-fda-orange-book-10272020 This first-ever Orange Book conference provided a roadmap to navigate and utilize the wealth of information the Orange Book contains, including therapeutic equivalence ratings, patents, exclusivities, and more. The conference featured Orange Book experts who provided insights and feedback related to the Orange Book's use and functionality, including possible future enhancements to the Orange Book.	October 27-28, 2020
FDA's Workshop: Non-clinical Immunogenicity Assessment of Generic Peptide Products: Development, Validation, and Sampling https://www.fda.gov/drugs/news-events-human-drugs/non-clinical-immunogenicity-assessment-generic-peptide-products-development-validation-and-sampling This workshop brought together global experts from industry, academia, and FDA to discuss the current regulatory thinking on and challenges with non-clinical assays for a comparative immunogenicity risk assessment for certain generic peptide products outlined in FDA's guidance for industry ***ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin*** (May 2021).	January 26, 2021
The FDA/SBIA Drug Master File (DMF) and Drug Substance Workshop www.fda.gov/drugs/news-events-human-drugs/drug-master-file-dmf-and-drug-substance-workshop-03032021-03042021 Through a series of presentations, panel discussions, and a Q&A for two poster sessions, this conference provided guidance on the DMF submission process and expectations for content. Ensuring high quality and manufacturing integrity of Active Pharmaceutical Ingredients (APIs) requires understanding and incorporation of quality and risk management principals throughout the API lifecycle. FDA outlined the various regulatory steps necessary for the successful development of a high-quality submission of drug substance information to the Agency.	March 3-4, 2021

FDA's Generic Drugs Forum 2021: Lifecycle of a Generic Drug www.fda.gov/drugs/news-events-human-drugs/generic-drugs-forum-2021-lifecycle-generic-drug-04282021-04292021 This forum updated industry stakeholders on the current trends related to GDUFA and FDA's generic drug program. Presentations by FDA offered practical advice, illustrated case studies, and enabled discussions about scientific issues related to ANDAs that were designed to help prospective generic drug developers reduce certain risks in their development programs and minimize the likelihood of deficiencies in their ANDAs.	**April 28-29, 2021**
FDA Webinar on Product-Specific Guidances: Lighting the Development Pathway for Generic Drugs www.fda.gov/drugs/fda-product-specific-guidances-lighting-development-pathway-generic-drugs-05052021-05052021 This was the first webinar on FDA's PSG program. It provided an overview of PSGs, including how they are developed and revised, as well as their role in facilitating generic drug development and ANDA review. FDA also discussed ways that prospective and current generic drug applicants can use PSGs, including those for complex products, to improve the efficiency of generic drug development.	May 5, 2021
FDA's Webinar: Common Labeling Deficiencies and Tips for Generic Drug Applications www.fda.gov/drugs/news-events-human-drugs/common-labeling-deficiencies-and-tips-generic-drug-applications-05072021-05072021 This webinar focused on the most common labeling mistakes found in ANDAs, discussed how to avoid them, and provided other labeling tips. FDA also answered common labeling questions asked by generic drug applicants.	May 7, 2021
FDA's FY 2021 Generic Drug Science and Research Initiatives Public Workshop www.fda.gov/drugs/news-events-human-drugs/fy-2021-generic-drug-science-and-research-initiatives-public-workshop-06232021-06232021 This science-focused public workshop provided an overview of ongoing work and outcomes from research advanced under the FY 2021 GDUFA	June 23, 2021

Science and Research Program priorities. A key objective of this workshop was to solicit public input related to the development of the following fiscal year's (i.e., FY 2022's) GDUFA science and research priorities. During the plenary session, the CRCG coordinated feedback from numerous generic drug industry stakeholders.	
FDA's Public Meeting on the Financial Efficiency of the Human Drug User Fee Program www.fda.gov/drugs/news-events-human-drugs/financial-transparency-and-efficiency-prescription-drug-user-fee-act-biosimilar-user-fee-act-and This meeting provided an update to public stakeholders on topics related to the financial management of user fee programs, including GDUFA II. FDA presented the 5-year financial plan and updated participants on its progress in implementing resource capacity planning, modernizing its time reporting approach, and addressing the findings (published in FY 2019) from an independent third-party evaluation of resource management for GDUFA.	June 28, 2021
The FDA/CRCG Workshop on In Vitro Release Test and In Vitro Permeation Test Methods: Best Practices and Scientific Considerations for ANDA Submissions www.fda.gov/drugs/news-events-human-drugs/fda-and-center-research-complex-generics-co-hosted-workshop-in-vitro-release-test-ivrt-and-vitro This workshop focused on scientific principles and practical considerations that inform FDA's current thinking and U.S. Pharmacopeia (USP) recommendations for in vitro release test and in vitro permeation test studies. This workshop included discussions on several challenging issues and areas needing further research, exploring opportunities for collaboration between FDA, USP, academic institutions, product manufacturers, diffusion cell equipment manufacturers, contract research organizations, consultants, and other stakeholders.	August 18-20, 2021

The FDA/SBIA Webinar on Manufacturing, Supply Chain, and Inspections During the COVID-19 Public Health Emergency www.fda.gov/drugs/news-events-human-drugs/manufacturing-supply-chain-and-inspections-during-covid19-public-health-emergency-08252021-08252021 In May 2021, FDA updated its August 2020 guidance for industry ***Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers*** to provide answers to frequently asked questions about regulatory and policy issues related to inspections, pending drug applications, and changes in manufacturing facilities for approved pharmaceutical products. This webinar provided the latest updates from the Center for Drug Evaluation and Research regarding policy and approaches toward manufacturing, supply chain, and inspections during the COVID-19 public health emergency.	**August 25, 2021**
The FDA/SBIA REdI Workshop on Advancing Generic Drug Development: Translating Science to Approval www.fda.gov/drugs/development-approval-process-drugs/cder-small-business-industry-assistance-sbia This public workshop communicated how outcomes from FDA's research conducted under GDUFA may guide and facilitate generic drug development, regulatory assessment, and approval. This workshop focused on common issues seen in ANDA submissions, linked GDUFA research outcomes to PSG development and pre-ANDA meeting discussions, and examined various areas of the science and cutting-edge methodologies behind drug development for generics, including complex generics.	September 20-21, 2021
The FDA/CRCG Workshop on Regulatory Utility of Mechanistic Modeling to Support Alternative Bioequivalence Approaches www.fda.gov/drugs/news-events-human-drugs/fda-and-center-research-complex-generics-co-hosted-workshop-regulatory-utility-mechanistic-modeling This workshop engaged generic industry stakeholders in discussing how mechanistic modeling and simulation can support generic product development and ANDA submissions, explored the current state of	September 29 - October 1, 2021

mechanistic modeling for BE assessments through case studies, discussed best practices for using physiologically based pharmacokinetic and computational fluid dynamics modeling to support an assessment of BE, and introduced the concept of a Model Master File to improve model-sharing between model developers, industry, and FDA.	

These and the many additional activities described in the 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

(This page left blank intentionally.)

Table of Contents

(This page left blank intentionally.)

Introduction

Millions of Americans use generic drugs to treat a wide variety of medical conditions.[21] FDA helps ensure that human generic drug products are thoroughly tested and shown to meet the statutory standards for approval, generally with evidence that these products 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 adherence to good manufacturing practice regulations as their brand-name counterparts.[22]

The Generic Drug User Fee Amendments (GDUFA) authorize 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, efficacy, and quality. 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 (FDARA) (Pub. L. 115-52)[23] into law, which included the Generic Drug User Fee Amendments of 2017 (GDUFA II). Under GDUFA II, FDA is continuing to modernize the generic drug program by improving its 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, FDA may grant requests for priority review for applications for generic drug products that are not blocked by patents or market exclusivities 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 communications and collaborations 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 or discipline review letters 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

[21] According to a report compiled by the Association for Accessible Medicines that was primarily based on data from IQVIA, generic drugs saved the American healthcare system nearly $2.4 trillion in the last 10 years due to the availability of affordable generics. The report is available at accessiblemeds.org/sites/default/files/2021-10/AAM-2021-US-Generic-Biosimilar-Medicines-Savings-Report-web.pdf.

[22] Some generic drugs are permitted, after the 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, and Cosmetic Act.

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

review cycle so that approval or tentative approval (TA) within the first cycle will be more achievable.

GDUFA II also introduced a pre-ANDA program designed to support the development of complex generic drug products, which features Product Development, Pre-Submission, and Mid-Review 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 the 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 communications 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 results in the fourth year of GDUFA II and presents the Agency's progress in accomplishing the FY 2021 program goals and enhancements of GDUFA II. Unless otherwise noted, all preliminary data for FY 2021 are as of September 30, 2021.

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 2021 may have associated goals in the subsequent fiscal year. In these cases, FDA's performance will be reported in the subsequent fiscal year.

- 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)).[24] 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

[24] www.fda.gov/media/101052/download.

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 2021, 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., a 10-month goal date in FY 2021) 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 of this report.

GDUFA II Workload

The table below summarizes the GDUFA II workload for FYs 2018, 2019 and 2020 and presents preliminary workload data for FY 2021.

GDUFA II Workload	FY 2018	FY 2019*	FY 2020	FY 2021
Original ANDAs				
Total Original ANDAs Submitted	1,044	909	865	810
ANDAs Submitted After RTR for Failure to Pay User Fees	16	14	10	7
ANDAs Submitted After RTR for Technical Reasons	81	51	42	47
ANDA Solicited Amendments				
Total Solicited ANDA Amendments Submitted	2,328	2,275	2,028	1,911
Prior Approval Supplements (PASs)				
Total PAS Submissions	1,103	889	1,133	1,351
PAS Solicited Amendments				
Total Solicited PAS Amendments Submitted	160	199	268	260
DMFs[†]				
Total DMFs Submitted	358	308	263	199
Controlled Correspondence (CC)				
Total CC Submitted	2,933	3,206	3,596	3,897

* Numbers were revised to reflect updates to the data presented in the FY 2020 GDUFA Performance Report.
[†] DMF submissions include only DMFs for which the holder has paid fees. Thus, the number of DMF submissions in a fiscal year will keep increasing as fees get paid.

GDUFA II 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 scheme not only streamlines the process but promotes more predictable timelines for actions.

FY 2021 Preliminary Performance

The table below reflects the GDUFA II 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 2021	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 the 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 (PAI) is not required)	8 months	90%	90%	90%	90%	90%
Standard Major ANDA Amendments (if PAI is required)	10 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if PAI is not required)	6 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if PAI is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority Major ANDA Amendments (if PAI 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 PAI is not required)	6 months	90%	90%	90%	90%	90%
Standard PAS (if PAI is required)	10 months	90%	90%	90%	90%	90%
Priority PAS (if PAI is not required)	4 months	90%	90%	90%	90%	90%
Priority PAS (if PAI is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority PAS (if PAI 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 PAI is not required)	6 months	90%	90%	90%	90%	90%
Standard Major PAS Amendment (if PAI is required)	10 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if PAI is not required)	4 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if PAI is required and applicant meets the requirements of a PFC)	8 months	90%	90%	90%	90%	90%
Priority Major PAS Amendment (if PAI 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§	Review and act on unsolicited ANDA amendments and PAS amendments 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.					

* Section I(1) of the GDUFA II Commitment Letter.
† Section I(B) of the GDUFA II Commitment Letter.
± Section I(C) of the GDUFA II Commitment Letter.
§ The GDUFA II Commitment Letter specifies reporting unsolicited amendments submitted during the review cycle and unsolicited amendments submitted between review cycles separately. For efficient treatment of these amendments, they are combined in this report.

GDUFA II provides review goals for certain DMF commitments and CC. The table below reflects these review goals for FYs 2018 to 2022.

GDUFA II Goals by Commitment Type	Review-Time Goal	FY 2018	FY 2019	FY 2021	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%

[#] For CC that raises an issue that relates to one or more pending citizen petitions, the 60- or 120-day time frame 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 2020 updated performance data and FY 2021 preliminary performance data. FDA continues to meet or exceed most of the review goals for the FY 2020 and 2021 cohorts. The "percent on time" column in the preliminary performance table for FY 2021 shows the percentage of submissions reviewed on time as of September 30, 2021, excluding action pending within the GDUFA review goal, and the "potential range" column shows the potential for meeting the FY 2021 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. These imminent approval performance numbers reflect FDA's decision to achieve an approval or TA within 60 days of the goal date rather than to act on the goal date, e.g., issue a CRL.

GDUFA FY 2020 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	667 of 684	95%	94% to 95%	97%	95% to 97%
Priority Original ANDA Submissions (if applicant meets requirements of a PFC)	8 months	31 of 31	97%	97% to 97%	97%	97% to 97%
Priority Original ANDA Submissions (if applicant does not meet requirements of a PFC)	10 months	127 of 133	97%	92% to 97%	97%	92% to 97%
Amendment Review						
Standard Major ANDA Amendments (if PAI is not required)	8 months	978 of 983	96%	96% to 96%	98%	98% to 98%
Standard Major ANDA Amendments (if PAI is required)	10 months	19 of 20	95%	95% to 95%	95%	95% to 95%
Priority Major ANDA Amendments (if PAI is not required)	6 months	166 of 167	95%	95% to 95%	97%	96% to 97%
Priority Major ANDA Amendments (if PAI is required and applicant meets the requirements of a PFC)	8 months	2 of 2	100%	100% to 100%	100%	100% to 100%
Priority Major ANDA Amendments (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	6 of 6	100%	100% to 100%	100%	100% to 100%
Standard and Priority Minor ANDA Amendments	3 months	851 of 852	93%	93% to 93%	99%	99% to 99%
Unsolicited ANDA Amendments	Varies	552 of 557	91%	90% to 91%	---	---
PAS Review Time						
Standard PAS (if PAI is not required)	6 months	960 of 963	99%	99% to 99%	99%	99% to 99%
Standard PAS (if PAI is required)	10 months	45 of 55	75%	75% to 75%	76%	76% to 76%
Priority PAS (if PAI is not required)	4 months	103 of 103	100%	100% to 100%	100%	100% to 100%
Priority PAS (if PAI is required and applicant meets the requirements of a PFC)	8 months	---	---	---	---	---
Priority PAS (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	7 of 7	100%	100% to 100%	100%	100% to 100%
PAS Amendments						
Standard Major PAS (if PAI is not required)	6 months	98 of 100	97%	95% to 97%	99%	97% to 99%
Standard Major PAS (if PAI is required)	10 months	3 of 5	60%	60% to 60%	60%	60% to 60%
Priority Major PAS (if PAI is not required)	4 months	9 of 9	100%	100% to 100%	100%	100% to 100%
Priority Major PASs (if PAI is required and applicant meets the requirements of a PFC)	8 months	---	---	---	---	---
Priority Major PASs (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	1 of 1	100%	100% to 100%	100%	100% to 100%
Standard and Priority Minor PAS Amendments	3 months	152 of 153	98%	98% to 98%	99%	99% to 99%
Unsolicited PAS Amendments	Varies	11 of 11	100%	100% to 100%	---	---
DMF						
Complete the initial completeness assessment review of Type II API DMF	60 calendar days	304 of 304	99%	99% to 99%	---	---

GDUFA FY 2020 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	3449 of 3464	98%	98% to 98%	---	---
Complex CC	120 calendar days	177 of 177	99%	99% to 99%	---	---
Clarification of Ambiguities in CC Response	14 calendar days	52 of 52	98%	98% to 98%	---	---

* Actions completed include any action taken regardless of whether it met the review-time goal. Even though no new submissions have come in (in the cohort year), the size of the cohort increases as the goal type is assigned.
† "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 FY 2021 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	71 of 520	99%	13% to 99%	100%	14% to 100%
Priority Original ANDA Submissions (if applicant meets requirements of a PFC)	8 months	14 of 36	100%	39% to 100%	100%	39% to 100%
Priority Original ANDA Submissions (if applicant does not meet requirements of a PFC)	10 months	13 of 119	93%	11% to 99%	100%	11% to 100%
Amendment Review						
Standard Major ANDA Amendments (if PAI is not required)	8 months	335 of 974	97%	34% to 99%	99%	34% to 99%
Standard Major ANDA Amendments (if PAI is required)	10 months	5 of 53	100%	9% to 100%	100%	9% to 100%
Priority Major ANDA Amendments (if PAI is not required)	6 months	69 of 142	93%	47% to 96%	99%	49% to 99%
Priority Major ANDA Amendments (if PAI is required and applicant meets the requirements of a PFC)	8 months	--	--	--	--	--
Priority Major ANDA Amendments (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	0 of 11	--	0% to 100%	--	0% to 100%
Standard and Priority Minor ANDA Amendments	3 months	515 of 710	91%	67% to 93%	99%	72% to 99%
Unsolicited ANDA Amendments	Varies	284 of 436	92%	61% to 94%	--	--
PAS Review Time						
Standard PAS (if PAI is not required)	6 months	673 of 1092	98%	61% to 98%	99%	62% to 99%
Standard PAS (if PAI is required)	10 months	17 of 72	85%	24% to 96%	100%	24% to 100%
Priority PAS (if PAI is not required)	4 months	102 of 119	100%	86% to 100%	100%	86% to 100%
Priority PAS (if PAI is required and applicant meets the requirements of a PFC)	8 months	0 of 2	--	0% to 100%	--	0% to 100%
Priority PAS (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	1 of 5	100%	20% to 100%	100%	20% to 100%
PAS Amendments						
Standard Major PAS (if PAI is not required)	6 months	45 of 88	98%	50% to 99%	98%	50% to 99%
Standard Major PAS (if PAI is required)	10 months	0 of 3	--	0% to 100%	--	0% to 100%
Priority Major PAS (if PAI is not required)	4 months	11 of 17	92%	65% to 94%	92%	65% to 94%
Priority Major PASs (if PAI is required and applicant meets the requirements of a PFC)	8 months	--	--	--	--	--
Priority Major PASs (if PAI is required and applicant does not meet the requirements of a PFC)	10 months	0 for 2	--	0% to 100%	--	0% to 100%
Standard and Priority Minor PAS Amendments	3 months	111 of 143	98%	76% to 99%	99%	77% to 99%
Unsolicited PAS Amendments	Varies	11 of 14	92%	79% to 93%		

GDUFA FY 2021 Preliminary Review Goals by Submission Type	Review Time Goal	Actions Complete*	Percent on Time†	Potential Range‡	On Time Imminent Approval	Imminent Approval Potential Range
DMF						
Complete the Initial Completeness Assessment Review of Type II API DMF	60 calendar days	412 of 412	98%	98% to 98%	--	--
CC						
Standard CC	60 calendar days	3256 of 3749	98%	86% to 98%	--	--
Complex CC	120 calendar days	182 of 259	95%	69% to 97%	--	--
Clarification of Ambiguities in CC Response	14 calendar days	35 of 37	94%	89% to 95%	--	--

* Actions completed include any action taken regardless of whether it met the review-time goal. Even though no new submissions have come in (in the cohort year), the size of the cohort increases as the goal type is assigned.

† "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's) 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	-	-	-	-	-
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	-	-	-	-	-

	Goal	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
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 2021

The following tables represent FDA's FY 2020 updated and FY 2021 preliminary performance results 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 2020 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	90%	5 of 5	100%	100% to 100%
Product Development Meetings					
FDA will grant or deny Product Development Meeting Requests	Within 14 calendar days from receipt of request	90%	99 of 99	100%	100% to 100%
FDA will conduct Product Development Meetings granted	Within 120 calendar days of granting them	80%	73 of 73	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	-	47 of 47	100%	100% to 100%
FDA will provide meeting minutes	Within 30 calendar days following the meeting	-	31 of 31	97%	97 to 97%
Pre-Submission Meetings					
FDA will grant or deny Pre-Submission Meeting Requests	Within 14 calendar days from receipt of request	90%	2 of 2	100%	100% to 100%
FDA will conduct Pre-Submission Meetings granted	Within 120 days of granting them	80%	1 of 1	100%	100% to 100%
If appropriate to the purpose of the meeting, FDA will provide preliminary written comments	5 calendar days before each meeting	-	1 of 1	100%	100% to 100%
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	-	5 of 5	100%	100% to 100%
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	-	118 of 118	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	-	343 of 343	95%	95% to 95%
FDA will decide whether to reclassify a major amendment or standard review status	Within 30 calendar days of the date of FDA's receipt of the request for a reclassification	90%	96 of 96	99%	99% to 99%

GDUFA II FY 2020 Updated Performance*	Review Goal	Goal	Actions Completed†	Percent on Time‡	Potential Range§
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	95%	95% to 95%
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	98%	98% to 98%
Safety Determination Letters					
FDA will issue safety determination letters	Within 60 calendar days of the date of submission of disclosure authorization	90%	3 of 3	100%	100% to 100%

* Numbers were changed to reflect updates to the data presented in the FY 2020 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 2021 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	90%	4 of 4	100%	100% to 100%
Product Development Meetings					
FDA will grant or deny Product Development Meeting Requests	Within 14 calendar days from receipt of request	90%	101 of 102	100%	99% to 100%
FDA will conduct Product Development Meetings granted	Within 120 calendar days of granting them	90%	72 of 77	99%	92% to 99%
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	--	40 of 50	98%	78% to 98%
FDA will provide meeting minutes	Within 30 calendar days following the meeting	--	27 of 31	100%	87% to 100%
Pre-Submission Meetings					
FDA will grant or deny Pre-Submission Meeting Requests	Within 14 calendar days from receipt of request	90%	5 of 5	100%	100% to 100%
FDA will conduct Pre-Submission Meetings granted	Within 120 days of granting them	90%	4 of 4	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	100%	100% to 100%
FDA will provide meeting minutes	Within 30 calendar days of the meeting	-	1 of 1	100%	100% to 100%
DMF First Cycle Review Deficiency					
FDA will strive to grant DMF first cycle review deficiency teleconferences	Within 30 calendar days	-	4 of 4	75%	75% to 75%
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	-	47 of 47	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	-	183 of 183	96%	96% to 96%
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%	64 of 66	97%	94% to 97%

GDUFA II FY 2021 Preliminary Performance	Review Goal	Goal	Actions* Completed	Percent on Time†	Potential Range‡
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%	73 of 73	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%	73 of 73	98%	98% to 98%
Safety Determination Letters					
FDA will issue safety determination letters§	Within 60 calendar days of the date of submission of disclosure authorization	90%	--	--	--

* 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.

§ The law commonly known as the "CREATES Act", enacted in December 2019 as part of the Further Consolidated Appropriations Act of 2020 (see FN 15, *supra*), makes available a new pathway for developers of potential drug and biological products to obtain samples of brand products that they need to support their applications. As part of CREATES implementation, FDA is no longer issuing the Safety Determination Letters to generic product developers that FDA had been issuing prior to CREATES under the draft guidance for industry *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD* (December 2014). Rather, FDA now issues Covered Product Authorizations under CREATES, which are accounted for under the complex CC GDUFA category.

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 2021, FDA published many guidances for industry[25] and Manuals of Policies and Procedures (MAPPs)[26] that provide important information for generic drug developers. These efforts support high-quality applications, streamlined application assessments, and ultimately can help facilitate faster generic drug approvals. In FY 2021, FDA published the following guidances for industry and MAPPs:

- Draft guidance for industry: *The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls* (October 2020)
- Final guidance for industry: *Referencing Approved Drug Products in ANDA Submissions* (October 2020)
- Final guidance for industry: *Formal Meetings Between FDA and ANDA Applicant of Complex Products Under GDUFA* (November 2020)
- Final guidance for industry: *Controlled Correspondence Related to Generic Drug Development*, December 2020
- Final guidance for industry: *Review Timelines for Applicant Responses to Complete Response Letters When a Facility Assessment Is Needed During the COVID-19 Public Health Emergency* (December 2020)
- Final guidance for industry: *Control of Nitrosamine Impurities in Human Drugs* (February 2021)
- Final guidance for industry: *Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Health Emergency* (April 2021)
- Final guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers* (May 2021)
- Final guidance for industry: *ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin* (May 2021)
- Final guidance for industry: *Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management* (May 2021)
- Final guidance for industry: *Field Alert Report Submission: Questions and Answers (July* 2021)
- Final guidance for industry: *Development and Submission of Near Infrared Analytical Procedures* (August 2021)
- Final guidance for industry: *Development of Abbreviated New Drug Applications During the COVID-19 Pandemic – Questions and Answers* (September 2021)

[25] FDA's guidance documents may be accessed at www.fda.gov/regulatoryinformation/guidances/.

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

- Final guidance for industry: *Questions and Answers on Quality Related Controlled Correspondence* (September 2021)
- Draft guidance for industry: *ICH Q12: Implementation Considerations for FDA-Regulated Products* (May 2021)
- Draft guidance for industry: *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations* (June 2021)
- Draft guidance for industry: *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application* (August 2021)
- Draft guidance for industry: *Microbiological Quality Considerations in Non-Sterile Drug Manufacturing* (September 2021)
- MAPP 5240.5 Rev 2: *ANDA Suitability Petitions* (October 2020)
- MAPP 5230.3 Rev 1: *Generic Drug Labeling Revisions Covered Under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act* (July 2021)

Pre-ANDA Program Goals – FY 2021 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 135 new and revised PSGs in FY 2021 (39 percent were for complex products).[27] The table below shows the FY 2021 PSG breakdown for complex and non-complex drug products.

	Complex Drug Products	Non-Complex Drug Products
Number of new PSGs	27	47
Number of revised PSGs	26	35
TOTAL	53	82

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

Since FY 2013, FDA has awarded 188 research contracts and grants. A complete list of FY 2018 through FY 2021 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
2021	16	18
2020	17	18
2019	20	25
2018	24	16

FY 2021 GDUFA Science and 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 toward generic drug product development and to contribute to

[27] The definition of a *complex product* can be found in Appendix A of this report.

general guidance development. FY 2021 GDUFA Science and Research Program includes the following 13 research areas:

- Abuse-Deterrent Opioid Drug Products
- Complex Injectables, Formulations, and Nanomaterials
- Complex Mixtures and Peptide Products
- Data Analytics
- Drug-Device Combination Products
- Inhalation and Nasal Products
- Locally Acting PBPK Modeling
- Long-Acting Injectable and Implant Products
- Ophthalmic Products
- Oral Absorption Models and BE
- Patient Substitution of Generic Drugs
- Quantitative Clinical Pharmacology
- Topical Dermatological Products

Key FY 2021 outcomes of each research program are highlighted in Appendix B of this report.

FY 2022 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 June 23, 2021, FDA held the FY 2021 Generic Drug Regulatory Science Initiatives Public Workshop, which provided an overview of the status of the generic drug regulatory science program and an opportunity for public input in developing the FY 2022 research priorities. Information obtained during the public workshop and other inputs, e.g., comments to the public docket, were considered in developing the FY 2022 GDUFA Science and Research Priority Initiatives.[28]

Following the public workshop, feedback and comments received at the workshop and through the docket resulted in the revision of several priority areas for FY 2022, including the expansion of priorities that reflect the current landscape of regulatory science needs. FDA will continue to track and report on these priority initiatives during the last year of GDUFA II. In each year of GDUFA II, FDA may revise the list and indicate when the priority initiatives are complete.

[28] The list of the FY 2022 research initiatives can be found at www.fda.gov/drugs/generic-drugs/generic-drug-research-priorities-projects.

The lists of research initiatives for earlier fiscal years are also available on FDA's Generic Drug Research Priorities and Projects webpage.[29]

The FY 2022 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 evaluations

A description of these topic areas and priorities is provided in Appendix C of this report.

[29] www.fda.gov/drugs/generic-drugs/generic-drug-research-priorities-projects.

Drug Safety and Inspections Performance

FDA is committed to ensuring consistency and transparency regarding inspections.

This section satisfies the annual reporting requirement created by the GDUFA II Commitment Letter for FY 2021 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 (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.

- Form FDA 483,[30] *Inspectional Observations*, is a 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.

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

- 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 (1) associated with an application that are not required to self-identify under GDUFA and (2) 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 a 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, an addition to an IA, or the holding of a Regulatory Meeting, could follow other types of inspections, though not typically as a result of 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, an addition to an IA, or the holding of a Regulatory Meeting. FDA notes 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.

- 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 FY 2021 inspections[31] conducted by domestic or foreign establishment locations, the 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 of 483s Issued**
PAI (API)**	1	11	12	8
PAI (API/FDF)**	1	1	2	2
PAI (FDF)**	25	5	30	23
PAI (Other)**	6	1	7	5
CGMP (API)	11	7	18	16
CGMP (API/FDF)	6	3	9	4
CGMP (FDF)	45	4	49	38
CGMP (Other)	29	0	29	19
BE Clinical**	15	6	21	5
BE Analytical**	0	0	0	0

* 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 (in calendar days) between the start of inspections and the issuance of a 483 in FY 2021.

[31] 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 U.S.-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.

Median Time from Beginning of Inspection to 483 Issuance in FY 2021

User Fee Program	FY 2021 Median Time (Calendar Days)
GDUFA	8.5

The following table shows the median time (in calendar days) in FY 2021 between the issuance of a 483 and the issuance of a WL, IA, and date of a Regulatory Meeting. This includes WLs, IAs, and 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 as 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) (Calendar Days)

User Fee Program	FY 2021 Median Time FDA 483 to WL	FY 2021 Median Time FDA 483 to IA	FY 2021 Median Time 483 to Reg. Meeting
GDUFA	215	125	234

The following table shows the median time (in calendar days) between the issuance or holding of a WL, IA, and Regulatory Meeting and OAI resolution in FY 2021. "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 2021 Median Time OAI Finalized to Resolution	FY 2021 Median Time WL to OAI Resolution	FY 2021 Median Time IA to OAI Resolution	FY 2021 Median Time Reg. Meeting to OAI Resolution
GDUFA	491	848	N/A	541

During FY 2021, there were seven facilities that were issued a WL and/or had a Regulatory Meeting with an OAI resolution occurring in or after FY 2018, the beginning of the GDUFA II reporting period. Four of these facilities were issued a WL and four had Regulatory Meetings. Resolution includes the firm addressing the CGMP violations or deviations that resulted in the OAI outcome, as well as a reinspection and classification of the site as VAI or NAI, when 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 it conducts inspections to verify pharmaceutical quality; the Agency also has improved transparency and timeliness in determining regulatory outcomes from inspections.[32]

In 2012, with the passage of the Food and Drug Administration Safety and Innovation Act,[33] 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 a determination that the foreign government has the capability to conduct inspections in accordance with section 809 of the Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA is currently implementing mutual recognition agreements (MRAs)[34] with the European Union (EU) and the United Kingdom (UK) that allow drug inspectors to rely upon information from drug inspections conducted within each other's borders. FDA expects to perform fewer routine surveillance inspections in foreign countries with a capable inspectorate. FDA, the EU, and the UK are now implementing these MRAs related to drug quality surveillance inspections. FDA accomplished the agreed-upon goal of making a capability determination for all EU member states and UK inspectorates of human drugs, including biologicals, by July 15, 2019. As a result of that accomplishment and as provided for in the FDA-EU MRA, the EU has stopped sampling and testing U.S.-produced drug batches distributed in the EU.

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

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

[34] See www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra.

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 declaration to an identified foreign regulator conveying the current CGMP compliance status for the establishment.

FDA met this goal in FY 2021 by responding within 30 days of receipt to three requests for CGMP declarations. (Seven total requests were received, and four requests did not fit the criteria for issuance.) In addition to CGMP declarations, there are other ways that FDA is enhancing communication and transparency with foreign regulatory authorities regarding the compliance status of establishments in the United States. For example, 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 UK, and the database now supports inclusion of facility status information based on the classification of inspection reports from foreign regulatory authorities.

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 FDA's 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, FY 2019, FY 2020 and FY 2021 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 (www.fda.gov/media/112562/download) on March 30, 2018.
FDA will implement methodologies for assessing resource needs of the program and for tracking resource utilization across the program elements.	Following the report review and comments	Methodology implemented.

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 an "Independent Evaluation of the GDUFA Resource Capacity Planning Adjustment Methodology" (www.fda.gov/media/140656/download) in July 2020.
FDA will use the results of the evaluation to create an ongoing financial reporting mechanism to enhance the transparency of GDUFA program resource utilization.		Implemented.
FDA will publish updates to the GDUFA Five-Year Financial Plan.	No later than the second quarter of each subsequent fiscal year	FDA published the FY 2021 GDUFA Five-Year Financial Plan update (www.fda.gov/about-fda/user-fee-reports/user-fee-five-year-financial-plans) in March 2021.
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 2021.

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 at www.fda.gov/industry/generic-drug-user-fee-amendments/enhanced-accountability-reporting.

FDA also committed to publishing more performance metrics in the annual GDUFA Performance Report. These further performance metrics either have 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, 2019, 2020, and 2021 receipt cohorts. These metrics include only 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*	FY 2020*	FY 2021
Receipt Cohort				
Mean Approval Time (Calendar Days)	584	511	374	287
Median Approval Time (Calendar Days)	522	472	351	296
Mean Tentative Approval Time (Calendar Days)	672	598	396	---
Median Tentative Approval Time (Calendar Days)	655	595	360	---
Mean Number of ANDA Review Cycles to Approval	2	2	2	1
Median Number of ANDA Review Cycles to Approval	2	2	1	1
Mean Number of ANDA Review Cycles to Tentative Approval	2	2	1	---
Median Number of ANDA Review Cycles to Tentative Approval	2	2	1	---

* Numbers were changed to reflect updates to the data presented in the FY 2020 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*	FY 2020*	FY 2021
Application Receipt				
Number of applications received	1044	909	865	810
Number of applications refused to receive	127	52	42	45
Average time to receipt decision (i.e., number of calendar days)	49	44	45	41
ANDA Review				
Number of ANDA applications received by FDA for standard review	555	569	648	499
Number of ANDA applications received by FDA for priority review	405	289	153	119
Percentage of ANDA proprietary name requests reviewed within 180 days of receipt	97%	89%	95%	94%
Petitions				
Number of suitability petitions pending a substantive response for more than 270 days from the date of receipt	136	161	172	173
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	2	5
DMF				
Number of DMF First Adequate Letters issued status (or equivalent)	189	198	213	254
Email Exchanges				
Number of initial (first cycle) email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in DMF deficiency letters	56	64	78	66
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	15	5

* Numbers were changed to reflect updates to the data presented in the FY 2020 GDUFA Performance Report.

Management Initiative	Performance Area	FY 2018	FY 2019	FY 2020	FY 2021
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.[35]	Teleconferences Requested	72	91	66	73
	Teleconferences Granted	56	67	55	56
	Teleconferences Denied	16	24	11	16
	Teleconferences Conducted	56	67	55	56
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	14	12	16
	Teleconferences Granted	24	11	12	16
	Teleconferences Denied	0	0	0	0
	Teleconferences Conducted	24	11	8	14
FDA will offer to hold a Mid-Review Cycle teleconference with an applicant if a Product Development or Pre-Submission Meeting has been held.[36]	Total Teleconferences	1	5	19	25
	Teleconferences Scheduled	1	5	19	20
	Teleconferences Conducted	1	5	15	5
FDA will strive to grant DMF first cycle review deficiency teleconferences	Teleconferences Requested	--	6	5	4
	Teleconferences Granted		6	4	0
	Teleconferences Denied		0	1	4
	Teleconferences Conducted		0	2	0

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

[36] 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.

Additional Reporting Requirements

Rationale for GDUFA Program Changes

FDARA amended the FD&C Act to require the reporting of certain information relating to GDUFA program changes in the annual performance report starting with FY 2020.

Requirements from Section 903 of FDARA

Specifically, section 903(c) of FDARA added section 744C(a)(3) of the FD&C Act, which requires that the annual GDUFA performance report include the following:

> (A) data, analysis, and discussion of the changes in the number of full-time equivalents hired as agreed upon in the letters described in section 301(b) of the Generic Drug User Fee Amendments of 2017 and the number of full-time equivalents funded by budget authority at the Food and Drug Administration by each division within CDER, the Center for Biologics Evaluation and Research (CBER), the Office of Regulatory Affairs (ORA), and the Office of the Commissioner (OC);
>
> (B) data, analysis, and discussion of the changes in the fee revenue amounts and costs for human generic drug activities, including identifying drivers of such changes; and
>
> (C) for each of the CDER, CBER, ORA, and OC, the number of employees for whom time reporting is required and the number of employees for whom time reporting is not required.

The information below fulfills these reporting requirements.

A. Changes in the Number of FTEs Hired As Agreed in the GDUFA Commitment Letter and the Number of FTEs Funded by Budget Authority by Division Within CDER, CBER, ORA, and OC

This section addresses the requirement to provide data, an analysis, and a discussion of the changes in the number of full-time equivalents (FTEs) hired as agreed upon in the letters described in section 301(b) of the Generic Drug User Fee Amendments of 2017 (GDUFA II) and the number of FTEs funded by budget authority at FDA by each division within CDER, CBER, ORA, and OC.

Changes in the Number of FTEs Hired

The GDUFA II Commitment Letter does not specify concrete hiring goals in terms of FTEs. However, in response to this reporting requirement, the Agency is providing the number of FTEs hired to meet the GDUFA II commitments, as indicated in the table below.

Number of FTEs Hired to Meet GDUFA II Commitments

Center	Number Hired in FY 2020	Number Hired in FY 2021	Change in Number Hired
CDER	40	10	-30
CBER	0	0	0
OC	0	0	0
ORA	29	6	-23
Total	69	16	-53

In prior reports, CDER had been reporting on the status of GDUFA II Loan FTEs. The majority of the temporary positions sunsetted in FY 2021 and were absorbed into the overall CDER Talent Acquisition Plan. The remaining GDUFA II Loan FTEs will sunset in FY 2022. The Talent Acquisition Plan will continue to help the Agency meet the goals outlined in the Commitment Letter.

FDA is focused on building staff capacity to manage the increasing program workload, meet performance goals, and deliver on new commitments funded in GDUFA II. The Agency continues to hire as needed to maintain staffing for the GDUFA program given attrition and the resources available to the program.

The change in number of FTEs reporting requirement (which was new for FY 2020) relates to changes in the number of FTEs hired "as agreed upon" in the GDUFA II Commitment Letter. Because the GDUFA II Commitment Letter did not include concrete FTE hiring goals, there was some variation in how the data were calculated and reported in the FY 2020 GDUFA Performance report. The table below has been updated from the FY 2020 report to reflect a harmonized approach to calculating the specified FY 2020 data.

Number of FTEs Hired to Meet GDUFA II Commitments

Center	Number Hired in FY 2019	Number Hired in FY 2020	Change in Number Hired
CDER	51	40	-11
CBER	0	0	0
OC	0	0	0
ORA	5	29	24
Total	56	69	13

Changes in the Number of FTEs Funded by Budget Authority by Division Within CDER, CBER, ORA, and OC

The data in the table below show the change from FY 2020 to FY 2021 in the number of FTEs funded by budget authority at FDA by each division within CDER, CBER, ORA, and OC. This table reflects the number of FTEs funded by budget authority for the GDUFA II program. For purposes of this table, "budget authority" refers to FDA's non-user fee annual appropriations. To address the requirement that information on the number of FTEs funded by budget authority be presented "by each division," the information in this table is broken down to the office level for the Centers, ORA, and OC. FDA uses a 2,080-hour workload to equate to one FTE, and this calculation is reflected in the table below. Data for FY 2021 and the previous year, FY 2020, are presented and compared to show the change in the number of FTEs over the last 2 fiscal years to directly support the GDUFA II program. The number of FTEs funded by budget authority for FY 2020 are those FTEs as of September 30, 2020. The number of FTEs funded by budget authority for FY 2021 are those FTEs as of September 30, 2021.

FDA reported a decrease in overall FTEs funded by budget authority in FY 2021 compared to FY 2020. The decrease in reported FTEs was attributable to re-baselining of payroll distribution percentages between annual appropriations and GDUFA fees.

Number of FTEs Funded by Budget Authority

Center and Office	Number of GDUFA Program FTEs Funded by Budget Authority*		Change in the Number of GDUFA Program FTEs Funded by Budget Authority
	FY 2020	FY 2021	
CDER			
Office of Communications	0.0	6.0	6.0
Office of Compliance	16.9	21.9	5.0
Office of the Center Director	1.1	6.7	5.6
Office of Executive Programs	1.2	0.4	-0.8
Office of Generic Drugs	16.1	7.2	-8.9
Office of Medical Policy	1.3	1.6	0.3
Office of Management	9.2	3.6	-5.6
Office of New Drugs	1.5	1.3	-0.2
Office of Pharmaceutical Quality	52.1	38.7	-13.4
Office of Regulatory Policy	8.2	8.5	0.3
Office of Surveillance and Epidemiology	32.7	9.3	-23.4
Office of Strategic Planning	21.6	17.8	-3.8
Office of Information Management and Technology	1.3	1.2	-0.1
Office of Translational Sciences	9.6	18.2	8.6
Other Offices	1.5	1.6	0.1
Working Capital Fund (WCF)	24.1	30.3	6.2
CBER			
Office of Biostatistics and Epidemiology	0.0	0.0	0.0
Office of Blood Research and Review	0.6	1.1	0.5
Office of Compliance and Biologics Quality	0.2	0.1	-0.1
Office of Communication Outreach and Development	0.1	0.1	0.0
Office of the Center Director	0.4	0.1	-0.3
Office of Management	0.2	0.2	0.0
WCF	0.1	0.1	0.0
ORA			
Office of Pharmaceutical Quality Operations	8.0	8.0	0
WCF	16.3	16.2	-0.1
OC			
OC Immediate Office	0.1	0.0	-0.1
Office of the Chief Counsel	0.8	0.2	-0.6
Office of the Chief Scientist	0	0	0

Center	Number of GDUFA Program FTEs Funded by Budget Authority*		Change in the Number of GDUFA Program FTEs Funded by Budget Authority
	FY 2020	FY 2021	
OC Continued			
Office of Clinical Policy and Programs	0.5	0	-0.5
Office of External Affairs	0.1	0	-0.1
Office of Global Policy and Strategy	0.6	0.1	-0.5
Office of Operations	0.7	0.3	-0.4
Office of Policy, Legislation, and International Affairs	0.5	0.1	-0.4
WCF	7.5	5.6	-1.9

*This table includes GDUFA program FTE calculated through WCF assessments for certain centrally administered services provided to CDER, CBER, ORA, and OC. Because many employees under OC and WCF do not report time, an average cost per OC and WCF FTE was applied to derive the number of GDUFA program FTEs funded by budget authority.

B. Changes in the Fee Revenue Amounts and Costs for the Review Process

Section 744C(a)(3) of the FD&C Act, as added by FDARA section 903(c), also requires that FDA provide data, analysis, and discussion of the changes in the fee revenue amounts and costs for human generic drug activities, including identifying drivers of such changes. Accordingly, the table below provides data for the GDUFA fee revenue amounts and process costs for FY 2020 and FY 2021, and the changes in these amounts from FY 2020 to FY 2021.

In FY 2021, FDA had net collections of $500 million in human generic drug user fees, spent $536 million in user fees for human generic drug activities, and carried a cumulative balance of $127 million forward for future fiscal years. Detailed financial information for the GDUFA user fee program can be found in the FY 2021 GDUFA financial report.

For FY 2018 through FY 2022, the base revenue amounts used in calculating the total GDUFA fee revenues are established by GDUFA II. For FY 2021, the base revenue amount is the FY 2020 inflation adjusted fee revenue amount of $513,223,160. The FY 2021 base revenue amount is then adjusted by inflation yielding a total adjusted fee revenue amount of $520,209,000 (rounded to the nearest thousand dollars). Actual collections were less than estimated collections in FY 2021.

In FY 2021, GDUFA costs decreased approximately $16 million from FY 2020. This decrease is attributed to lower spending, an Agency redistribution of shared services costs by funding source, and a drop in ORA's operating costs.

Changes in the Fee Revenue Amounts and Review Process Costs

Fiscal Year	FY 2020	FY 2021	Change from FY 2020 to FY 2021
Fee Revenue Amounts (Net Collections)	$483,285,782	$500,205,882	+3%
Review Process Cost	$698,085,185	$681,916,125	-2%

C. Number of Employees for Whom Time Reporting Is Required

Section 744C(a)(3) of the FD&C Act, as added by FDARA section 903(c), also requires that FDA provide for each of the CDER, CBER, ORA, and OC, the number of employees for whom time reporting is required and the number of employees for whom time reporting is not required. Accordingly, the table below provides the number of employees within CDER, CBER, ORA, and OC who are required to report their time and those who are not required to report their time as of September 30, 2021.

These data reflect time reporting across all employees in each entity, rather than only those engaged in GDUFA program activities.

Time Reporting Requirement for FY 2021

Center	FTEs for Whom Time Reporting Is Required	FTEs for Whom Time Reporting Is Not Required
CDER	5,315	45
CBER	1,194	18
ORA	3,111	1,804
OC	41	2,609
Total	9,661	4,476

(This page left blank intentionally.)

Appendices

Appendix A: Definitions of Key Terms

A. **Act on an Application** means that FDA will 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.[37]

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.

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

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 CDER's December 2020 guidance for industry *Controlled Correspondence Related to Generic Drug Development*.[38] 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.

---

[38] www.fda.gov/media/109232/download.

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 of an ANDA to CDER's Office of Generic Drugs or CBER.

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.[39]

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.

[39] 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. **Reference Listed Drug (RLD)** means the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA.

Y. **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).[40]

Z. **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.

AA. **Standard controlled correspondence (CC)** means controlled correspondence:

1. As described in CDER's December 2020 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.

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

CC. **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* (February 2020).[41]

DD. **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

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

[41] Ibid.

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.

EE. **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: Significant FY 2021 GDUFA Science and Research Accomplishments

Significant FY 2021 GDUFA science and research accomplishments are highlighted below with a key FY 2021 outcome for each of the 13 research programs:

- **ABUSE-DETERRENT OPIOID DRUG PRODUCTS**

  In vitro and in vivo studies were performed, which provided mechanistic, clinically meaningful insights about the role of excipients in products that may be abused. In vivo studies in guinea pigs identified that one such excipient, high molecular weight polyethylene oxide, was associated with a risk of kidney damage. Subsequent in vitro studies were initiated to develop efficient tools that could both test formulations with such excipients and reproduce the mechanistic effects that may correlate with in vivo kidney damage.

- **COMPLEX INJECTABLES, FORMULATIONS, AND NANOMATERIALS**

  In vitro studies were performed that systematically characterized the influence of manufacturing conditions on the arrangement of matter in liposomal Amphotericin B. These studies not only revealed how the manufacturing process changed the molecular state of the drug and its association with the lipid shell of the liposome but also elucidated how this modulated the drug release. These manufacturing tools provide a simple and powerful way to optimize the manufacturing conditions for complex generics with nanotechnology to ensure that these generics are safe and effective.

- **COMPLEX MIXTURES AND PEPTIDE PRODUCTS**

  In vitro and in silico studies were performed to develop efficient ways to anticipate or characterize impurities that can arise in oligonucleotide or peptide drug products. These studies will help the development of PSGs for such products, which will facilitate the development and approval of generics in this evolving class of therapeutics.

- **DATA ANALYTICS**

  Research exploring artificial intelligence (AI) methods successfully developed a novel tool that can assist FDA scientists who collect and organize large amounts of detailed scientific information to be reviewed; this novel tool will allow them to assess whether the information supports specific regulatory decisions. By automating the systematic collection and organization of this comprehensive set of scientific information, such AI tools have the potential to substantially improve the efficiency and consistency with which FDA may be able to assess all the relevant information, which can help streamline the development of PSGs for generic product development and support other regulatory decision-making.

- **DRUG-DEVICE COMBINATION PRODUCTS**

  In vivo studies involving patients with asthma and chronic obstructive pulmonary disease provided new insights into patient perceptions about generic dry powder inhalers; these perceptions can help (1) identify and characterize potential differences in the user interface of generic drug-device combination products and (2) evaluate how such differences may affect the risk of user medication errors when a patient switches from

using the brand name product to a generic. These studies also identified opportunities for improving generic drug literacy among adults, adolescents, and healthcare providers.

- **INHALATION AND NASAL DRUG PRODUCTS**

  In vitro and in vivo studies were performed to clarify whether differences in the characteristics of dry powders (drugs) that are inhaled into the lung (which cause orally inhaled drug particles to deposit in different regions of the lung) can be differentiated by efficient plasma or serum pharmacokinetic studies. The result of these studies indicated both that pharmacokinetic parameters can be sensitive to differences in regional lung deposition of a drug and that this sensitivity may be dependent on specific parameters for dry powder inhalers.

- **LOCALLY ACTING PBPK MODELING**

  An extensive literature search was performed to characterize the differences in anatomy and physiology between animals (like rabbits) and humans, as well as to identify scientific issues that may otherwise limit the extrapolation of animal data to humans. These anatomical and physiological parameters (e.g., tear film volume, tera flow rate, aquoues humor volume, surface area of conjunctiva, etc.) were incorporated into PBPK models that have the potential to help predict human ocular pharmacokinetics and pharmacodynamics through interspecies extrapolation by PBPK modeling and thereby support the development of locally acting ophthalmic generics, which are highly challenging to study in humans. Additionally, an open-source ophthalmic model database has been created and it is currently available publicly (https://eye.health-map.net/).

- **LONG-ACTING INJECTABLES AND IMPLANTED PRODUCTS**

  In vitro studies were performed that revealed that injectable suspensions can be highly sensitive to the shear forces produced when such formulations get injected; the reversible flocculation or deflocculation of drug particles was highly dependent upon the differences in shear. Since deflocculated particles may dissolve up to six times faster than the flocculated particles, these studies suggested that differences in shear forces during the administration of injections may have the potential to substantially alter bioavailability and, if not controlled, may increase the variability in product performance.

- **OPHTHALMIC DRUG PRODUCTS**

  A novel in vitro release test (IVRT) method involving adaptive perfusion was developed based upon tangential flow filtration principles; this method provided size-based separation of particulates with a simultaneous analysis of the released drug and the remaining drug. Using this novel IVRT method, discriminatory drug release profiles were obtained in solutions, micelles, and nanoemulsions of small, medium, and large size globules. Sensitive and discriminating IVRT methods like this can facilitate comparative assessments of product quality and performance, which can support efficient demonstrations of BE.

- **ORAL ABSORPTION MODELS AND BE**

  A review of relevant literature describing the differences in the relative bioavailability between adult and pediatric populations indicated that particular care is needed for Biopharmaceutics Classification System Class II drugs and narrow therapeutic index

drugs, when assessing the BE of products used in a pediatric population. Biorelevant dissolution methods were explored for several drugs that have been studied in both adults and children, and these drugs' dissolution profiles are being integrated into PBPK modelling to determine whether these methods provide suitable discriminatory tools to better predict BE for children based upon studies performed in adults.

- **PATIENT SUBSTITUTION OF GENERIC DRUGS**

  The rising cost in recent decades of inhaled corticosteroid and long acting β agonist combination products has led to concerns about equitable patient access to these products. The availability of generic alternatives for such products can improve patient access to more affordable, high quality, and safe and effective medicines. To understand the potential impact of generics for such products, an analysis of pharmacoeconomic data was performed, which revealed that the first generic fluticasone propionate and salmeterol xinafoate dry powder inhaler was associated with up to $1 billion in drug cost-savings for this class of medications during the first year of market availability.

- **QUANTITATIVE CLINICAL PHARMACOLOGY**

  Research into the development of model-integrated strategies for generic long-acting injectable and implantable products indicated that one of the advantages of using the model-integrated approach is that it can increase statistical power while handling differences in the rate and extent of drug absorption with an adequately controlled Type 1 error. In addition, this approach can account for uncertainties related to the model structure and parameters. This research demonstrated the plausibility of innovative BE study designs to facilitate the development of long-acting injectable generic products.

- **TOPICAL DERMATOLOGICAL PRODUCTS**

  In vitro studies were performed to understand the impact of differences in manufacturing processes, as well as the corresponding differences in the physicochemical and structural properties of topical gels, on the release and bioavailability of tretinoin from topical gels with nanotechnology microparticles. The results indicated that it is essential to understand the manufacturing processes of a topical microparticle gel because manufacturing differences may alter the quality and performance of such gels. Also, the novel in vitro characterizations developed as part of this research may provide a tool to facilitate product development and may be critical to the development of a characterization-based BE approach for this nanotechnology product and similar ones.

Appendix C: FY 2022 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. For FY 2022, several priority areas were revised and new priorities that reflect the current landscape of regulatory science needs were added. For example, FDA received general feedback that research to support global harmonization of the most efficient BE standards should be prioritized. In addition, several generic industry stakeholders emphasized the need for research on harmful impurities such as nitrosamines, potentially related to their formation or mitigation, the development of computational toxicology tools, and the assessment of human exposure risks. The scientific considerations associated with harmful impurities such as nitrosamines are not specific to generic products, but, given the number of prescriptions filled by generic medications, this is a high priority for generic product manufacturers.

FDA also received feedback about the need for tools to facilitate the prediction of both lung tissue concentrations and systemic concentrations of orally inhaled products, suggesting a need for research to link validated computational fluid dynamics (CFD) models to mechanistic PBPK models; this feedback also suggested a need for research utilizing CFD modeling to explore the relationship between aerodynamic particle size distribution (APSD) and regional lung deposition for various orally inhaled products, and to calibrate the cascade impactor studies that are used to derive APSDs. In addition, FDA received specific feedback that results from dissolution tests may have limitations for informing PBPK and pharmacokinetic/pharmacodynamic models that are intended to support a demonstration of BE, and that research is needed to potentially also integrate the results from permeability studies into these models.

Another area where FDA received feedback related to prioritizing research into the utilization of AI to enhance and expedite the development and assessment of generic drugs. Discussions during the FY 2021 Generic Drug Science and Research Initiatives Public Workshop illustrated that AI tools are already utilized by certain generic industry stakeholders that confirmed the current utility and future potential of AI to support generic drug development and assessment. Further research was recommended to establish how AI can support the assessment of prospective 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 orthogonal methods for characterization of chemical compositions, molecular structures, and distributions of complex active ingredients

2. Improve particle size, shape, and surface characterization to support demonstration of therapeutic equivalence of suspended and colloidal drug products

3. Establish predictive in silico, in vitro, and animal models to evaluate 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 and drug release mechanisms for these products

5. Advance characterization tools for polymeric excipients and related complex formulations to provide product-specific guidance on qualitative sameness assessment and explore alternative BE approaches.

B - Complex routes of delivery

1. Improve PBPK and CFD models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic) to allow their use in supporting alternative BE approaches

2. Enhance understanding of the role of excipients in topical drug absorption to evaluate in vitro BE methods for these topical drug products applied to skin or other local areas that are not qualitatively (Q1) the same or quantitatively (Q2) similar in inactive ingredients as compared to their reference products

3. Implement in vitro methods together with pharmacokinetic and certain other methods as alternatives to the use of comparative clinical endpoint BE studies for nasal and inhaled drug products

C - Complex drug-device combination products

1. Evaluate the impact of identified differences in the user-interface from the RLD on the therapeutic equivalence and post-marketing safety 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 evaluations

1. Improve quantitative pharmacology and BE trial simulation to optimize the design of BE studies for generic drug products and establish a foundation for model-based BE study designs

2. Integrate predictive dissolution and permeability test results, PBPK models, pharmacokinetic/ pharmacodynamic models, and machine learning to evaluate in vitro BE options for orally administered drug products, to support global harmonization of the most efficient BE recommendations, or to assess the risk of human exposure to harmful impurities such as nitrosamine

3. Expand the scientific understanding of the role of excipients in generic drug products, either related to the formation or mitigation of harmful impurities such as nitrosamines or to support the expansion of the Biopharmaceutics Classification System Class

III biowaivers for drug products with differences in formulations larger than currently recommended in FDA's guidance documents

4. Develop alternative BE approaches to account for unexpected events such as COVID-19-related study interruptions and protocol deviations

5. Develop methods and integrated technological solutions that will allow FDA to leverage AI tools and large data sets (such as the development of models and data to support quantitative structure-activity relationship-based methods for harmful impurities such as nitrosamines, BE study submissions, electronic health records, substitution/utilization patterns, drug safety data, and drug quality data) to support regulatory decisions and to improve the post-market surveillance of generic drug substitutions

Appendix D: Analysis of Use of Funds

On August 18, 2017, FDARA (Pub. L. 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. These 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 the 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 2020 Final Performance	Review Goal	Received	Received with Goal Post FY 2020	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
I. Original ANDA Review Goals									
Standard Original ANDA Applications	10 months	648	566	95	17	517	32	95%	94% to 95%
Priority Original ANDA Applications (if applicant meets requirements of a PFC)	8 months	31	17	8	0	23	1	97%	97% to 97%
Priority Original ANDA Applications (if applicant does not meet the requirements of a PFC)	10 months	122	111	24	3	89	4	97%	92% to 97%
II. Amendment Review Goals									
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	983	702	165	37	774	38	96%	96% to 96%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	20	17	7	1	11	1	95%	95% of 95%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	167	96	40	4	122	8	95%	95% to 95%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	2	2	0	0	2	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	6	4	1	0	5	0	100%	100% to 100%

Goal Type FY 2020 Final Performance	Review Goal	Received	Received with Goal Post FY 2020	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
Standard and Priority Minor ANDA Amendments	3 months	852	213	405	112	333	62	93%	93% to 93%

* Missed Goals include submissions that have not had an action and have passed the goal date.
† These percentages include RTR actions, withdrawn submissions, and pending submissions, in addition to approval, TA, and CR actions.

Goal Type FY 2021 Preliminary Performance	Review Goal	Received	Received with Goal Post FY 2021	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
I. Original ANDA Review Goals									
Standard Original ANDA Applications	10 months	495	455	9	0	36	1	99%	13% to 99%
Priority Original ANDA Applications (if applicant meets requirements of a PFC)	8 months	32	23	1	0	9	0	100%	39% to 100%
Priority Original ANDA Applications (if applicant does not meet the requirements of a PFC)	10 months	116	108	1	0	8	1	93%	11% to 99%
II. Amendment Review Goals									
Standard Major ANDA Amendments (if pre-approval inspection is not required)	8 months	974	653	34	5	293	9	97%	34% to 99%
Standard Major ANDA Amendments (if pre-approval inspection is required)	10 months	53	50	0	0	5	0	100%	9% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	142	72	10	1	58	5	93%	47% to 96%
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant meets the requirements of a PFC)	8 months	--	--	--	--	--	--	--	--
Priority Major ANDA Amendments (if pre-approval inspection is required and applicant does not meet the requirements of a PFC)	10 months	11	11	0	0	0	0	--	0% to 100%
Standard and Priority Minor ANDA Amendments	3 months	710	201	265	60	190	48	91%	67% to 93%

* 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 letter described in section 301(b) of GDUFA II (i.e., currently the 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	www.fda.gov/drugs/drug-approvals-and-databases/most-recent-changes-iid-database
Complete enhancements to the Inactive Ingredient Database so users can perform electronic queries to obtain accurate Maximum Daily Intake and Maximum Daily Exposure information for each route of administration for which data is available.	10/1/2021	Y	Enhancements published 07/30/2021	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 6/23/2021	www.fda.gov/drugs/news-events-human-drugs/fy-2021-generic-drug-science-and-research-initiatives-public-workshop-06232021-06232021
Hold meetings between FDA and industry's GDUFA II regulatory science working group.	Biannually	Y	First Meeting held 3/12/2021 Second Meeting held 9/24/2021	www.fda.gov/drugs/generic-drugs/generic-drugs-priorities-projects
Report on its website the extent to which GDUFA regulatory science-funded projects support the development of generic drug products, the generation of evidence needed to support the efficient review and timely approval of ANDAs, and the evaluation of generic drug equivalence.	Annually	Y	Posted 11/22/2021	www.fda.gov/drugs/generic-drugs/gdufa-science-and-research-outcomes-fiscal-year-2020
Issue PSGs identifying the methodology for developing drugs and generating evidence needed to support ANDA approval for 90 percent of new chemical entity New Drug Applications that are approved on or after October 1, 2017, at least 2 years prior to the earliest lawful ANDA filing date.	At least 2 years prior to the earliest lawful ANDA filing date.	Y	Annual	In FY 2019, 36 non-complex new chemical entity New Drug Applications were approved. FDA has issued PSGs for all 36 non-complex new chemical entities (www.accessdata.fda.gov/scripts/cder/psg/index.cfm)
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 www.fda.gov/drugs/abbreviated-new-drug-application-anda/generic-drugs-program-activities-report-monthly-performance

Performance Enhancement Goal	Target Goal Date	On Time (Y/N)	Actual Completion Date	Comments
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 www.fda.gov/industry/generic-drug-user-fee-amendments/activities-report-generic-drugs-program-gdufa-ii-quarterly-performance
Publish annual reporting metrics set forth under section VI(C)(3)(a) through (p) of the GDUFA II Commitment Letter	Annually	Y	Annual	Please see the Performance Reporting section of the FY 2021 GDUFA Performance Report
Publish updates to the GDUFA Five-Year Financial Plan no later than the second quarter of each subsequent fiscal year	3/31/2021	Y	3/31/2021	FDA published the FY 2021 GDUFA Five-Year Financial Plan update in March 2021 (www.fda.gov/media/147060/download)
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	6/30/2021	Y	6/22/2021	FDA held the public meeting (Financial Transparency and Efficiency of GDUFA) in June 2021 to discuss the GDUFA Five-Year Financial Plan

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.

In addition to the causes and trends initially identified in last year's report, the table below represents FDA's FY 2020 updated performance results.

Cause or Trend	Impact on FDA's Ability to Meet Goals
Review Goals	In last year's report, the Agency could not fully report on this category in the Appendix because some submissions received in FY 2020 had associated review goals that fell within the subsequent fiscal year (i.e., in FY 2021). As promised in last year's report, the Agency is now able to fulfill the commitment to fully report its performance review goals. FDA did not meet the FY 2020 review goals for Standard PAS (when a PAI was required) and Standard Major PAS Amendment (when a PAI was required). Standard PAS (when a PAI was required) and Standard Major PAS Amendment (when a PAI was required) goals were affected by travel restrictions related to the COVID-19 public health emergency and its impact on FDA's inspections.
Review Program Enhancement Goals	In last year's report, the Agency could not fully report on this category in the Appendix because some submissions received in FY 2020 had associated review program enhancement goals that fell within the subsequent fiscal year (i.e., in FY 2021). As promised in last year's report, the Agency is now able to fulfill the commitment to fully report its performance on review program enhancement goals. FDA met the FY 2020 review program enhancement goals.
Pre-ANDA Program Goals	In last year's report, the Agency could not fully report on this category in the Appendix because some submissions received in FY 2020 had associated pre-ANDA program goals that fell within the subsequent fiscal year (i.e., in FY 2021). As promised in last year's report, the Agency is now able to fulfill the commitment to fully report its performance on pre-ANDA program goals. FDA met the FY 2020 pre-ANDA program goals.

The table below represents FDA's FY 2021 preliminary performance results.

Cause or Trend	Impact on FDA's Ability to Meet Goals
Review Goals	Some submissions received in FY 2021 have associated review goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review goals, FDA will provide a full evaluation next year.

Cause or Trend	Impact on FDA's Ability to Meet Goals
Review Program Enhancement Goals	Some submissions received in FY 2021 have associated review program enhancement goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review program enhancement goals, FDA will provide a full evaluation next year.
Pre-ANDA Program Goals	Some submissions received in FY 2021 have associated pre-ANDA program goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 pre-ANDA program goals, FDA will provide a full evaluation next year.

Appendix E: FY 2021 Corrective Action Report

FY 2021 Corrective Action Report

On August 18, 2017, FDARA (Pub. L. 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.[42]

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.

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

Executive Summary

FY 2020 Review Goal Performance

The following table represents FDA's FY 2020 updated performance results for goal types that the Agency was not able to fully report on in last year's report. If a goal type is not listed in this table for FY 2020, then the Agency fully reported on it in last year's report.[43]

Goal Type	Circumstances and Trends Impacting the Ability to Meet the Goal Date	Corrective Action Plan
Review Goals	Standard PAS (when a PAI was required) and Standard Major PAS Amendment (when a PAI was required) goals were affected by travel restrictions related to the COVID-19 public health emergency and its impact on FDA's inspections.	FDA is continuing to strive to meet all GDUFA review goal dates while ensuring the health, safety, and well-being of its investigators. In FY 2021, FDA continued to conduct mission-critical and prioritized inspections and increased its use of alternative approaches to inspections, to the extent possible, to reduce the need to conduct PAIs and to meet GDUFA review goal dates.
Review Program Enhancement Goals	All FY 2020 goals were met.	No corrective action plan is needed.
Pre-ANDA Program Goals	All FY 2020 goals were met.	No corrective action plan is needed.
Facilities Goals	All FY 2020 goals were met.	No corrective action plan is needed.
Enhanced Accountability and Reporting Goals	All FY 2020 goals were met.	No corrective action plan is needed.
Policy Documents	All FY 2020 goals were met.	No corrective action plan is needed.
Public Meetings and Workshops	All FY 2020 goals were met.	No corrective action plan is needed.
Program and Process Implementation	All FY 2020 goals were met.	No corrective action plan is needed.
Reporting	All FY 2020 goals were met.	No corrective action plan needed.
Website Publishing	All FY 2020 goals were met.	No corrective action plan is needed.

[43] See www.fda.gov/about-fda/user-fee-performance-reports/gdufa-performance-reports.

The following table represents FDA's FY 2021 preliminary performance results.

Goal Type	Circumstances and Trends Impacting the Ability to Meet the Goal Date	Corrective Action Plan
Review Goals	Too soon to determine.	Some submissions received in FY 2021 have associated review goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review goals, FDA will provide a full evaluation next year.
Review Program Enhancement Goals	Too soon to determine.	Some submissions received in FY 2021 have associated review program enhancement goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review program enhancement goals, FDA will provide a full evaluation next year.
Pre-ANDA Program Goals	Too soon to determine.	Some submissions received in FY 2021 have associated pre-ANDA program goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 pre-ANDA program goals, FDA will provide a full evaluation next year.
Facilities Goals	All FY 2021 goals were met.	No corrective action plan is needed.
Enhanced Accountability and Reporting Goals	All FY 2021 goals were met.	No corrective action plan is needed.
Policy Documents	All FY 2021 goals were met.	No corrective action plan is needed.
Public Meetings and Workshops	All FY 2021 goals were met.	No corrective action plan is needed.
Program and Process Implementation	All FY 2021 goals were met.	No corrective action plan is needed.
Reporting	All FY 2021 goals were met.	No corrective action plan needed.
Website Publishing	All FY 2021 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 FDA to provide a justification for the determination of review goals missed during FYs 2020 and 2021 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 2020 Review Goal Performance

A. Summary of Performance: A small number of submissions for the Standard PAS (when a PAI was required) and Standard Major PAS Amendment (when a PAI was required) review goals were missed during FY 2020.

B. Justification: These goals were affected by travel restrictions related to the COVID-19 public health emergency and its impact on FDA's inspections.

C. FY 2021 Corrective Actions: FDA is continuing to strive to meet all GDUFA review goal dates while ensuring the health, safety, and well-being of its investigators. In FY 2021, FDA continued to conduct mission-critical and prioritized inspections and increased its use of alternative approaches to inspections, to the extent possible, to reduce the need to conduct PAIs and meet GDUFA review goal dates.

II. FY 2021 Review Goal Performance

A. Summary of Performance: Some submissions received in FY 2021 have associated review goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review goals, FDA will provide a full evaluation next year.

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

C. FY 2021 Corrective Actions: Too soon to determine if a corrective action is needed.

III. FY 2021 Review Program Enhancement Goals

A. Summary of Performance: Some submissions received in FY 2021 have associated review program enhancement goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 review program enhancement goals, FDA will provide a full evaluation next year.

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

C. *FY 2021 Corrective Actions:* Too soon to determine if a corrective action is needed.

IV. FY 2021 Pre-ANDA Goals Performance

A. *Summary of Performance:* Some submissions received in FY 2021 have associated pre-ANDA goals that fall within the subsequent fiscal year (i.e., in FY 2022). Because FDA cannot yet evaluate the entire performance for FY 2021 pre-ANDA goals, FDA will provide a full evaluation next year.

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

C. *FY 2021 Corrective Actions:* Too soon to determine if a corrective action is needed.

V. FY 2021 Facilities Goals Performance

A. *Summary of Performance:* All FY 2021 goals were met.

B. *Justification:* No justification is needed.

C. *FY 2021 Corrective Actions:* No corrective action is needed.

VI. FY 2021 Enhanced Accountability and Reporting Goals Performance

A. *Summary of Performance:* All FY 2021 goals were met.

B. *Justification:* No justification is needed.

C. *FY 2021 Corrective Actions:* No corrective action is needed.

VII. FY 2021 Policy Documents

A. *Summary of Performance:* All FY 2021 goals were met.

B. *Justification:* No justification is needed.

C. *FY 2021 Corrective Actions:* No corrective action is needed.

VIII. FY 2021 Public Meetings and Workshops

A. *Summary of Performance:* All FY 2021 goals were met.

B. *Justification:* No justification is needed.

C. *FY 2021 Corrective Actions:* No corrective action is needed.

IX. FY 2021 Program and Process Implementation

A. Summary of Performance: All FY 2021 goals were met.

B. Justification: No justification is needed.

C. FY 2021 Corrective Actions: No corrective action is needed.

X. FY 2021 Website Publishing

A. Summary of Performance: All FY 2021 goals were met.

B. Justification: No justification is needed.

C. FY 2021 Corrective Actions: No corrective action is needed

XI. Reporting

A. Summary of Performance: All FY 2021 goals were met.

B. Justification: No justification is needed.

C. FY 2021 Corrective Actions: No corrective action is needed.

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 it 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 2021.

This section presents non-review performance goals cited in the GDUFA II Commitment Letter with required completion dates in FY 2021. 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 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 2021 is necessary.

This report was prepared by FDA's Office of Planning in collaboration with FDA's Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research. For information on obtaining additional copies, contact:

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

This report is available on FDA's home page at www.fda.gov.