U.S. FOOD & DRUG ADMINISTRATION

FY 2018

PERFORMANCE REPORT TO CONGRESS

for the

Generic Drug User Fee Amendments

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Acting Commissioner's Report

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

FDA's early investments to improve the timeliness and predictability of the generic drug application review process have produced a strong foundation that has benefited the public health. Under GDUFA I, FDA executed a deep, foundational restructuring of the generic drug program that included hiring and training over 1,000 employees, overhauling the program's business processes, and developing and implementing an integrated generic drug application review platform.

Over the course of the GDUFA program, FDA has reduced review times for new generic drug applications, approved a record number of generic drug applications, and met or exceeded a majority of the performance goals while maintaining the Agency's high approval standards. Under GDUFA II, FDA is continuing to modernize the generic drug program by improving the program's efficiency, quality, and predictability.

In 2017, FDA's Drug Competition Action Plan (DCAP) was launched to promote competition and access to affordable generic drug products. Under DCAP, FDA has focused efforts on three key areas: (1) improving the efficiency of generic drug development, review, and approval processes; (2) maximizing scientific and regulatory clarity with respect to generic versions of complex drug products; and (3) closing loopholes that allow brand drug companies to "game" the Hatch-Waxman Amendments in ways that forestall the generic competition that Congress intended.

We are confident that new processes introduced through GDUFA II and activities taken under DCAP will help reduce review cycles, continue to improve approval times, and boost competition for the American public.

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

Norman E. Sharpless, M.D.
Acting Commissioner of Food and Drugs

Acronyms

ANDA – Abbreviated New Drug Application

API – Active Pharmaceutical Ingredient

BE – Bioequivalence

CA – Completeness Assessments

CC – Controlled Correspondence

CBER – Center for Biologics Evaluation and Research

CDER – Center for Drug Evaluation and Research

CGMP – Current Good Manufacturing Practice

CR – Complete Response

CRL - Complete Response Letter

DMF – Drug Master File

DRL – Discipline Review Letter

ECD – Easily Correctable Deficiency

eCTD – Electronic Common Technical Document

EU – European Union

FDA – Food and Drug Administration

FDARA – FDA Reauthorization Act of 2017

FDASIA – Food and Drug Administration Safety and Innovation Act

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

FDF – Finished Dosage Form

FY – Fiscal Year (October 1 – 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

IR – Information Request

IT – Information Technology

MAPP – Manual of Policies and Procedures

NAI – No Action Indicated

OAI – Official Action Indicated

OGD – Office of Generic Drugs

ORA – Office of Regulatory Affairs

PAI – Pre-Approval Inspection

PAS – Prior Approval Supplement

PFC – Pre-Submission Facility Correspondence

RLD – Reference Listed Drug

RPM – Regulatory Project Manager

RTR – Refuse to Receive

TA – Tentative Approval

UL – Untitled Letter

VAI – Voluntary Action Indicated

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Executive Summary

On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA),[1] which included the authorization of the Generic Drug User Fee Amendments of 2012 (GDUFA). GDUFA authorized the Food and Drug Administration (FDA or the Agency) to collect user fees for human generic drug activities and enabled FDA to advance a safer, more efficient, and more affordable human generic drug review program.

Each iteration of GDUFA has covered a 5-year period, and Congress may choose to reauthorize future versions of GDUFA. On August 18, 2017, the President signed into law the FDA Reauthorization Act of 2017 (FDARA),[2] 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 identify opportunities for earlier and enhanced communication to support the efficient and effective pre-market review of generic drugs. Such communication is critical for FDA to meet the new, shorter review goals negotiated under GDUFA II for generic drug submissions that are public health priorities. These shorter review goals and communication enhancements are supported by an overall user fee structure that is consistent with FDA's anticipated workload and that will better address challenges facing small businesses.

A key feature of GDUFA II is the pre-Abbreviated New Drug Application ("pre-ANDA") program, which was designed to support development of complex generic drug products. The pre-ANDA program features product development, pre-submission, and mid-review cycle meetings to help clarify regulatory expectations early in product development and during application review.

FDA made noteworthy advancements in the implementation of GDUFA II. This annual report presents preliminary data on FDA's success in meeting fiscal year (FY) 2018 review goals and commitments for GDUFA II and updates the review goals for FY 2017, the final year of GDUFA I.

Highlighted Achievements – FY 2018

The goals negotiated by FDA and the generic drug industry under GDUFA II are set forth in the document titled "GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022," which is referred to as the GDUFA II Commitment Letter.[3] The bulleted list below highlights FDA's performance with respect to a select sample of the GDUFA II goals. The list also highlights some notable achievements made by the Agency in FY 2018.

In many instances, FDA has taken actions beyond the goals in the GDUFA II Commitment Letter when the Agency believes that taking such actions will help increase access to affordable generic drug products. These actions may include, for example, issuing guidance to support development of generic drug products, engaging industry in meetings to provide clarification that

[1] www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf
[2] www.congress.gov/115/plaws/publ52/PLAW-115publ52.pdf
[3] www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/ucm525234.pdf

can help lead to faster approvals, and the activities taking place under DCAP. The rest of this report provides a more comprehensive evaluation of the Agency's performance in FY 2018.

During FY 2018, FDA accomplished the following:

- FDA approved 781 ANDAs and tentatively approved 190 ANDAs,[4] the highest number of combined generic drug approvals and tentative approvals (TA) in the history of the generic drug program. FDA has set new records during each of the last 3 years.

- Under GDUFA II, FDA committed to review and act on 90 percent of standard original ANDAs within 10 months of the date of ANDA submission. As of September 30, 2018, FDA has met 96 percent of the goals for such applications.

- As of September 30, 2018, FDA has not missed a single goal for priority original ANDA submissions with an 8-month goal date.[5]

- As of September 30, 2018, FDA met 98 percent of the goals pertaining to Prior Approval Supplements (PASs).

- In an effort to improve predictability and transparency, promote the efficiency and effectiveness of the review process, and minimize the number of review cycles necessary for approval, FDA issued 4,452 Information Requests (IRs) and 2,048 Discipline Review Letters (DRLs).

- Under GDUFA II, FDA committed to review and respond to 90 percent of all standard controlled correspondence (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 2,933 CCs during FY 2018, a number that has tripled since the beginning of GDUFA.[6] Even with the substantial increase, as of September 30, 2018, FDA continues to exceed the goals for 99 percent of all standard CC and 98 percent of all complex CC.

- FDA issued 11 draft guidances and 5 final guidances for industry, not including product-specific guidances. The FY 2018 guidances include a draft guidance titled *Formal Meetings between FDA and ANDA Applicants of Complex Products under GDUFA*,[7] a draft guidance titled *Good ANDA Submission Practices*, and the final guidance for industry *ANDA Submissions – Amendments to Abbreviated New Drug Applications Under GDUFA*. FDA publishes regulatory 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.

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[4] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm625314.htm.

[5] Under GDUFA II, FDA committed to review and act on 90 percent of priority original ANDAs within 8 months of the date of ANDA submission, if the applicant meets the requirements of a Pre-Submission Facility Correspondence (PFC).

[6] FDA received the following numbers of CC: 953 in FY 2013; 1,089 in FY 2014; 1,472 in FY 2015; 1,883 in FY 2016; and 2,667 in FY 2017.

[7] www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm578366.pdf. This guidance and all other guidances (except the product specific guidances) can be found at: www.fda.gov/RegulatoryInformation/Guidances/default.htm.

- FDA posted 136 new draft guidances and 72 revised draft guidances with product-specific recommendations[8] in FY 2018. These draft guidances describe the Agency's current thinking and draft recommendations on how to develop generic drug products therapeutically equivalent to specific reference-listed drugs.

- FDA issued seven Manuals of Policies and Procedures (MAPPs), including MAPP 5241.3[9] – "Good Abbreviated New Drug Application Assessment Practices" and revised MAPP 5240.3[10] – "Prioritization of the Review of Original ANDAs, Amendments, and Supplements." MAPPs document internal FDA policies and procedures and are accessible to the public to make FDA's operations more transparent. The MAPPs highlighted in this report define FDA's policies, responsibilities, and procedures as they relate to FDA's generic drug program.

- FDA engaged in outreach efforts to educate and inform industry participants and other stakeholders about GDUFA and the generic drugs program. For example: in November 2017, FDA speakers, along with industry, addressed key regulatory and technical issues impacting the generic drug industry and FDA at the Association for Accessible Medicines' (AAM) Fall Technical Conference.[11] FDA produced webinars[12] for the Center for Drug Evaluation and Research's (CDER) Small Business and Industry Assistance (SBIA), corresponding to and discussing five GDUFA II draft guidances, including *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* and *Information Requests (IR) and Discipline Review Letters (DRL) Under GDUFA*.

- FDA held a new education event for industry, the "SBIA Complex Generic Drug Products Conference" (September 12-13, 2018). This conference provided detailed scientific advice for complex generic drug development and drew 3,253 total registrants in its first year.

- FDA held six regulatory science public meetings and workshops focusing on complex generic drug development, including "Demonstrating Equivalence of Generic Complex Drug Substances and Formulations"[13] (October 2017) and "FY 2018 Generic Drug Regulatory Science Initiatives Public Workshop"[14] (May 2018).

- During the April 2018 "Regulatory Education for Industry Generic Drugs Forum,"[15] FDA staff discussed strategies for industry to provide high-quality submissions to FDA and GDUFA regulatory science research with the generic drug industry and other stakeholders. Attendance was up 40 percent from 2017, with more than 3,100 registrants.

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[8] www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm075207.htm.
[9] www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM591143.pdf.
[10] www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM407849.pdf.
[11] accessiblemeds.org/FallTech2017.
[12] www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm604924.htm.
[13] www.fda.gov/drugs/newsevents/ucm552461.htm
[14] www.fda.gov/Drugs/NewsEvents/ucm583766.htm.
[15] www.fda.gov/drugs/developmentapprovalprocess/smallbusinessassistance/ucm598753.htm.

- In FY 2018, FDA recorded the podcast "U.S. Generic Drug Policy: Less Cost, Same Impact"[16] and held a four-part webinar series on complex generic drug development in partnership with the Drug Information Association (DIA), including "An Overview of Challenges and Opportunities in the Development of Complex Generic Drug Products"[17] and "Overcoming Barriers to Entry for Complex Generic Oral Inhalation Drug Products."[18]

- In FY 2018, FDA-supported research resulted in over 50 peer reviewed publications related to generic drugs. These publications, such as *Effects of Formulation Variables on Lung Dosimetry of Albuterol Sulfate Suspension and Beclomethasone Dipropionate Solution Metered Dose Inhalers*, which was published in *AAPS*[19] *PharmSciTech*, aid the generic drug industry in developing high quality generic products.

[16] www.diapublications.podbean.com/e/us-generic-drug-policy-less-cost-same-impact/.
[17] www.diaglobal.org/general/play-product-video?ProductID=7259905&_ga=2.160810749.1926118028.1529501166-349294289.1522761792.
[18] www.diaglobal.org/general/play-product-video?ProductID=7259905&FileType=AWS&FileSpec=RA_OGD_WebinarMarch15th.mp4&_ga=2.80086871.1926118028.1529501166-349294289.1522761792.
[19] American Association of Pharmaceutical Scientists

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Introduction

Millions of Americans use generic drugs to treat a wide variety of medical conditions.[20] The Food and Drug Administration (FDA or the Agency) helps ensure that human generic drug products are thoroughly tested and shown to meet the statutory standards for approval, generally with evidence that they contain the same active ingredients, route of administration, labeling, strength, and dosage form; deliver the same amount of active ingredients to the site of action; and maintain the same strict standards of good manufacturing practice regulations as their brand-name counterparts.[21]

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

Since the implementation of GDUFA in fiscal year (FY) 2012, FDA has met or exceeded a majority of its goals without compromising its high standards regarding safety, quality, and transparency. GDUFA has provided the mechanism necessary to secure the resources needed to gain efficiencies, promote innovation, and enhance the overall generic drug review process.

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

GDUFA II also includes increased communication and collaboration between FDA and industry to help improve the quality of submissions and identify, earlier in the process, potential issues that could impact approval of an application. For example, under GDUFA II, FDA issues Information Requests (IRs) or Discipline Review Letters (DRLs) during the review of an original Abbrievated New Drug Application (ANDA) when further information or clarification is needed or would be helpful to allow completion of a discipline review or to convey preliminary thoughts on possible deficiencies. These tools allow applicants to address some issues within the original review cycle so that approval or Tentative Approval (TA) within the first cycle is more achievable.

GDUFA II also introduced a pre-ANDA program designed to support development of complex generic drug products, which features product development, pre-submission and mid-review cycle meetings to help clarify regulatory expectations early in product development and during application review.

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[20] According to a report compiled by the QuintilesIMS Institute on behalf of AAM, generic drugs saved the American health care system $1.67 trillion over the 10-year period from 2007 through 2016—with over $253 billion saved in 2016 alone. The report is available at www.accessiblemeds.org/sites/default/files/2017-07/2017-AAM-Access-Savings-Report-2017-web2.pdf.

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

Under GDUFA II we are also taking steps to foster earlier development of guidance, including product-specific guidances, 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 review goals cover a wide range of improvements including: enhancing communication between FDA and industry throughout the review process; enhancing communications regarding inspections of facilities and sites; improving predictability and transparency; promoting the efficiency and effectiveness of the review process; enhancing Drug Master File (DMF) reviews; enhancing accountability and reporting; and advancing regulatory science initiatives. This report details FDA's performance in the first year of GDUFA II and presents the Agency's progress in accomplishing the final year's program goals and enhancements detailed in GDUFA I. Unless otherwise noted, all preliminary data for FY 2018 are as of September 30, 2018.

The information below provides some key terms and concepts used in this report.

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

FY 2018 where the Agency worked past a goal date rather than issuing a complete response letter by the goal date to resolve outstanding issues with the ANDA and issued an approval or TA. As a result of these efforts under this program enhancement commitment, FDA has reduced the number of review cycles necessary for approval of these applications and facilitated more timely access to generic drug products. FDA intends to report on imminent approvals and imminent TAs in subsequent performance reports as each GDUFA II review cohort matures (i.e., next year we intend to provide this information for the FY 2018 cohort when we provide the final performance data for this cohort).

- For a review goal to be met, FDA must review the specified percentage of submissions within the review goal. For example, in FY 2018, to meet the goal for standard original ANDAs, FDA must review and act on 90 percent within 10 months.
- To "act on an application" means that FDA will issue a Complete Response letter (CRL), an approval letter, a TA letter, or a refuse to receive (RTR) letter.
- Submission types with shorter review goals (e.g., standard and priority minor ANDA amendments with 3-month goal dates) tend to have a larger percentage of reviews completed by the end of the fiscal year, and their preliminary performance is a more reliable indicator of their final performance. However, submission types (e.g., standard original ANDA submissions) with longer review goals (e.g., 10-month goal date in FY 2018) tend to have a smaller percentage of reviews completed, 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.

Review Workload: FYs 2017 and 2018

The tables below summarize GDUFA workload for FY 2017 and present preliminary workload data for FY 2018.

GDUFA I Workload	FY 2017
Original ANDAs	
Total Original ANDAs Submitted	1,310
ANDAs Submitted after RTR for Failure to Pay User Fees	13
ANDAs Submitted after RTR for Technical Reasons	152
ANDA Solicited Amendments	
Total Solicited ANDA Amendments Submitted	23[22]
PASs	
Total PAS Submissions with Inspection Status Undetermined	411
PAS Solicited Amendments	
Total Solicited PAS Amendments Submitted	29
CC	
Total CC Submitted	2,637
Total CC Requiring Input from Clinical Division	29

GDUFA II Workload	FY 2018
Original ANDAs	
Total Original ANDAs Submitted	1,044
ANDAs Submitted after RTR for Failure to Pay User Fees	16
ANDAs Submitted after RTR for Technical Reasons	78
ANDA Solicited Amendments	
Total Solicited ANDA Amendments Submitted	2,330
PASs	
Total PAS Submissions	1,103
PAS Solicited Amendments	
Total Solicited PAS Amendments Submitted	168
DMF	
Total DMFs Submitted and Completed	401
CC	
Total CC Submitted	2,933

[22] NOTE: This FY17 value is low because it reflects solicited amendments from just FY 17, not the total of all amendments received during the FY. Under GDUFA II, amendments are now considered part of the cohort for the fiscal year the amendment is submitted. For FY18, the value is higher because it represents the total number of solicited amendments received, regardless of the FY of original ANDA receipt.

GDUFA Review Goals

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

GDUFA II Review Goals – FY 2018 Preliminary Performance

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

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

*Commitment Letter - I(A)
†Commitment Letter - I(B)
±Commitment Letter - I(C)

GDUFA II also provides new review goals for certain DMF commitments, controlled correspondence, and ANDAs bridged from GDUFA I. The table below reflects these review goals for FYs 2018 - 2022.

GDUFA II Goals/Commitment Type	Review-Time Goal	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
DMF						
Complete the initial completeness assessment review of Type II Active Pharmaceutical Ingredient (API) Drug Master Files (DMFs)	Within 60 days of the later of the date of DMF submission or DMF Fee payment[§]	90%	90%	90%	90%	90%
CC [‡‡]						
Standard CC	Within 60 days of submission date[§]	90%	90%	90%	90%	90%
Complex CC	Within 120 days of submission date[§]	90%	90%	90%	90%	90%
Submitter requests to clarify ambiguities in the CC	Within 14 days of request receipt[§]	90%	90%	90%	90%	90%
GDUFA I Bridging[§§]						
Continue to review and act on ANDAs and ANDA Amendments submitted prior to October 1, 2017	10 months	90%	--	--	--	--

[§]These metrics refer to calendar days.
[‡‡]In the case of CC that raises an issue that relates to one or more pending citizen petitions, the 60- or 120-day timeframe starts on the date FDA responds to the petition (if there is only one petition) or last pending petition.
[§§]ANDA Original Submissions and Amendments to those submissions that did not receive a GDUFA I review goal or a Target Action Date (TAD), or did not receive a TAD, and remained pending in the same review cycle as of October 1, 2017, received an appropriate GDUFA II review goal on October 1, 2017, which did not exceed July 31, 2018.

The following table represents FDA's preliminary performance on the GDUFA II review goals for FY 2018. The percent on time column shows the percentage of submissions reviewed on time as of September 30, 2018, excluding action pending within the GDUFA review goal, and the potential range column shows the potential for meeting the FY 2018 GDUFA review goal.

GDUFA II Review Goals by Submission Type	Review Goal	Actions Completed	Percent on Time	Potential Range
Original ANDA Review				
Standard Original ANDA Submissions	10 months	72 of 503	96%	14% to 99%
Priority Original ANDA Submissions (if applicant meets requirements of a PFC)	8 months	10 of 36	100%	28% to 100%
Priority Original ANDA Submissions (if applicant does not meet requirements of a PFC)	10 months	101 of 387	96%	25% to 99%
Amendment Review				
Standard Major ANDA Amendments (if preapproval inspection is not required)	8 months	226 of 752	96%	29% to 99%
Standard Major ANDA Amendments (if preapproval inspection is required)	10 months	0 of 32	--	0% to 100%
Priority Major ANDA Amendments (if preapproval inspection is not required)	6 months	92 of 280	99%	32% to 100%
Priority Major ANDA Amendments (if preapproval inspection is required and applicant meets the requirements of a PFC)	8 months	--	--	--
Priority Major ANDA Amendments (if preapproval inspection is required and applicant does not meet the requirements of a PFC)	10 months	0 of 10	--	0% to 100%
Standard and Priority Minor ANDA Amendments	3 months	834 of 1,234	93%	64% to 95%
Unsolicited ANDA Amendments (In Cycle)	Varies	129 of 206	98%	63% to 98%
Unsolicited ANDA Amendments (Between Cycles)	Varies	7 of 20	88%	35% to 95%
PAS Review Time				
Standard PAS (if preapproval inspection is not required)	6 months	425 of 666	99%	63% to 99%
Standard PAS (if preapproval inspection is required)	10 months	10 of 28	100%	36% to 100%
Priority PAS (if preapproval inspection is not required)	4 months	36 of 50	97%	70% to 98%
Priority PAS (if preapproval inspection is required and applicant meets the requirements of a PFC)	8 months	--	--	--
Priority PAS (if preapproval inspection is required and applicant does not meet the requirements of a PFC)	10 months	1 of 3	100%	33% to 100%
PAS Amendments				
Standard Major PAS Amendment (if preapproval inspection is not required)	6 months	26 of 48	100%	54% to 100%
Standard Major PAS Amendment (if preapproval inspection is required)	10 months	0 of 2	--	0% to 100%
Priority Major PAS Amendment (if preapproval inspection is not required)	4 months	3 of 8	67%	25% to 88%
Priority Major PAS Amendment (if preapproval inspection is required and applicant meets the requirements of a PFC)	8 months	--	--	--
Priority Major PAS Amendment (if preapproval inspection is required and applicant does not meet the requirements of a PFC)	10 months	--	--	--
Standard and Priority Minor PAS Amendments	3 months	88 of 106	99%	82% to 99%
Unsolicited PAS Amendments (In Cycle)	Varies	10 of 13	100%	77% to 100%
Unsolicited PAS Amendments (Between Cycles)	Varies	--	--	--
DMF				
Complete the initial completeness assessment review of Type II API DMF	Within 60 days of the later of the date of DMF submission or DMF Fee payment	383 of 383	96%	96% to 96%
CC	120 calendar days	87 of 147	98%	58% to 99%
Standard CC	60 calendar days	2,432 of 2,789	99%	87% to 99%
Complex CC	120 calendar days	87 of 147	98%	58% to 99%
Clarification of Ambiguities in Controlled Correspondence Response	14 calendar days	25 of 27	92%	89% to 93%
GDUFA Bridging				
Continue to review and act on ANDAs and ANDA Amendments submitted prior to October 1, 2017	Varies	1,016 of 1,037	96%	94% to 96%

GDUFA I Review Goals

The following table shows the final performance for the FY 2017 cohort. The data shows that FDA met or exceeded a majority of the goals for the FY 2017 cohort.

GDUFA I FY 2017 Updated Performance	Review Goal	Goal	Actions* Completed	Percent on Time†	Potential Range‡
I. Original ANDA Review-Time Goals					
Original ANDA Applications	10 months	90%	1,299 of 1,310	96%	95% to 96%
II. Amendment Review-Time Goals					
Tier 1 - First Major Amendments	10 months	90%	2 of 2	100%	100% to 100%
Tier 1 - First through Third Minor Amendments	3 months	90%	22 of 22	77%	77% to 77%
Tier 1 - First through Third Minor Amendments Requiring an Inspection	10 months	90%	--	--	--
Tier 1 - Fourth through Fifth Minor Amendments	6 months	90%	--	--	--
Tier 1 - Fourth through Fifth Minor Amendments Requiring an Inspection	10 months	90%	--	--	--
Tier 1 - Unsolicited Delaying Amendments	3 months	90%	32 of 32	100%	100% to 100%
Tier 2 Amendments	12 months	90%	8 of 8	88%	88% to 88%
Tier 3 Amendments	**--**	**--**	--	--	--
III. PAS Review-Time Goals					
PASs Not Requiring Inspections	6 months	90%	388 of 388	98%	98% to 98%
PASs Requiring Inspections	10 months	90%	23 of 23	96%	96% to 96%
IV. PAS Amendment Review-Time Goals					
Tier 1 - First Major Amendments	10 months	90%	3 of 3	100%	100% to 100%
Tier 1 - First through Third Minor Amendments	3 months	90%	22 of 22	95%	95% to 95%
Tier 1 - First through Third Minor Amendments Requiring Inspection	10 months	90%	**--**	**--**	**--**
Tier 1 - Fourth through Fifth Minor Amendments	6 months	90%	**--**	**--**	**--**
Tier 1 - Fourth through Fifth Minor Amendments Requiring Inspection	10 months	90%	**--**	**--**	**--**
Tier 1 - Unsolicited Delaying Amendments	3 months	90%	3 of 3	67%	67% to 67%
Tier 2 Amendments	12 months	90%	2 of 2	100%	100% to 100%
Tier 3 Amendments	--	--	**--**	**--**	**--**
V. CC					
CC	2 months	90%	2,628 of 2,639	99%	98% to 99%
CC Requiring Input from Clinical Division	3 months	90%	29 of 29	100%	100% to 100%

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

GDUFA I - Review Time

The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) required FDA to report the average total time to full approval action of applications (original ANDAs and PASs) received in each fiscal year cohort.

This metric requires FDA to report the average total time to full approval action for ANDAs and PASs[23] received during the respective fiscal year, including the number of calendar days spent during the review by FDA and the number of calendar days spent by the applicant responding to a CRL(s). The figures represented under each cohort are revised annually to incorporate updated results based on ANDAs and PASs approved in the previous fiscal year. The data are presented in the following two tables. (Note that the time-to-approval is dropping for the newer applications.)

Average Calendar Days to Full Approval Action: Original ANDAs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
First Cycle Approvals*					
Average Total Time to Approval	1,142	961	467	457	310
Multi-Cycle Approvals					
Average Total Time to Approval	1,349	1,175	857	707	490
Average Time Spent During Review by FDA	1,084	995	656	610	426
Average Time Spent by Applicant Responding to CR	265	181	201	98	64
Total Combined (First Cycle and Multi-Cycle)					
Combined Average Total Time to Approval	1,315	1,093	780	618	411

* First cycle approvals may include applications for which Easily Correctable Deficiencies (ECDs) and IRs were issued to help applicants correct deficiencies in the current review cycle. This reduces the need for additional review cycles; however, it may add to the total review time for first cycle approvals.

[23] FDASIA added section 715(a)(2) to the FD&C Act, which requires FDA to report on the average total time for "applications for approval of a generic drug under 505(j), amendments to such applications, and prior approval supplements…" Pursuant to 21 CFR 314.96, applicants may amend an ANDA not yet approved to revise existing information or provide additional information. When calculating time to approval, amendments are combined with an original ANDA or PAS. Thus, a metric specific to amendments is not included as the time FDA spends reviewing amendments is already captured in the time to approval of an ANDA or PAS.

Average Calendar Days to Full Approval Action: PASs

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
First Cycle Approvals*					
Average Total Time to Approval	363	296	111	112	121
Multi-Cycle Approvals					
Average Total Time to Approval	753	744	522	442	339
Average Time Spent During Review by FDA	594	537	295	269	256
Average Time Spent by Applicant Responding to CR	159	206	227	173	83
Total Combined (First Cycle and Multi-Cycle)					
Combined Average Total Time to Approval	460	373	197	173	150

* First cycle approvals may include supplements for which ECDs and IRs were issued to help applicants correct deficiencies in the current review cycle. This reduces the need for additional review cycles; however, it may add to the total review time for first cycle approvals.

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 - 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 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	-	-	-	-	-
FDA conduct teleconferences that an applicant requests as part of its request to reclassify a major amendment or standard review status.	Within 30 calendar days of date of FDA's receipt of the request for a teleconference	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 2018

The following tables represent FDA's preliminary performance on the GDUFA II program enhancement goals for FY 2018. 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 on 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 review of a generic drug submission; however, it is important that FDA meet its pre-submission meeting goals and other program enhancement goals to support efficient reviews and more generic drug approvals.

GDUFA II FY 2018 Preliminary Performance	Review Goal	Goal	Actions* Completed	Percent on Time†	Potential Range‡
Dispute Resolution					
FDA will respond to appeals above the Division level	30 days	70%	34 of 35	100%	97% to 100%
Product Development Meetings					
FDA will grant or deny Product Development Meeting Requests	30 days	90%	65 of 71	98%	92% to 99%
FDA will conduct Product Development Meetings granted	120 days	60%	22 of 43	100%	51% 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 days	-	19 of 33	100%	58% to 100%
FDA will provide meeting minutes	30 days	-	9 of 21	100%	43% to 100%
Pre-Submission Meetings					
FDA will grant or deny Pre-Submission Meeting Requests	30 days	90%	12 of 12	100%	100% to 100%
FDA will conduct Pre-Submission Meetings granted	120 days	60%	3 of 5	100%	60% to 100%
If appropriate to the purpose of the meeting, FDA will provide preliminary written comments	5 days	-	4 of 4	75%	75% to 75%
FDA will provide meeting minutes	30 days	-	2 of 3	100%	67% to 100%
DMF First Cycle Review Deficiency					
FDA will strive to grant DMF first cycle review deficiency teleconferences	30 days	-	10 of 10	30%	
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	14 days	-	23 of 23	43%	43% to 43%
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	14 days	-	20 of 20	95%	95% to 95%
FDA will schedule and conduct teleconferences that an applicant requests as part of its request to reclassify a major amendment or standard review status.	30 days	90%	195 of 198	99%	96% to 99%
Post-CRL					
FDA will provide a scheduled date for a requested Post-CRL teleconference	10 days	90%	53 of 53	92%	92% of 92%
FDA will conduct requested post-CRL teleconferences on the FDA-proposed date	30 days	90%	53 of 53	100%	100% to 100%
Safety Determination Letters					
FDA will issue safety determination letter	60 days	90%	5 out of 5	100%	100% to 100%

Additional Activities to Promote Transparency and Enhance Communications

FDA committed to increasing transparency and communication between FDA and generic drug developers. In addition to the GDUFA II commitments outlined above, in FY 2018 FDA went beyond these commitments by publishing many guidances for industry and MAPPs, which provide important information for generic drug developers. This information supports high quality applications, streamlined application assessments, and ultimately faster generic drug approvals. In FY 2018, FDA published the following guidances[24] and MAPPs[25]:

- Draft Guidance for Industry: ANDA Submissions – Refuse-to-Receive Standards: Questions and Answers, October 2017
- Draft Guidance for Industry: Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA, October 2017
- Draft Guidance for Industry: ANDAs for Certain Highly Purified Synthetic Peptide Drug Products that Refer to Listed Drugs of rDNA Origin, October 2017
- Final Guidance for Industry: Completeness Assessments for Type II API DMFs Under GDUFA Guidance for Industry, October 2017
- Final Guidance for Industry: ANDA Submissions – Prior Approval Supplements Under GDUFA, October 2017
- Draft Guidance for Industry: Requests for Reconsideration at the Division Level Under GDUFA, October 2017
- Draft Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application, October 2017
- Draft Guidance for Industry: Assessing User Fees Under the Generic Drug User Fee Amendments of 2017, October 2017
- Draft Guidance for Industry: Post-Complete Response Letter Meetings Between FDA and ANDA Applicants, October 2017
- MAPP 5220.1: Receiving and Processing a Request for Voluntary Withdrawal of an Approved ANDA, October 2017
- MAPP 5200.12: Communicating Abbreviated New Drug Application Review Status Updates with Industry, October 2017
- Draft Guidance for Industry: Controlled Correspondence Related to Generic Drug Development, November 2017

[24] FDA guidances may be accessed at www.fda.gov/regulatoryinformation/guidances/.
[25] CDER MAPPs may be accessed at www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/default.htm.

- Draft Guidance for Industry: ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications (Pre-Submission Facility Correspondence), November 2017
- Final Guidance for Industry: General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products, November 2017
- MAPP 5240.3 Rev. 4: Prioritization of the Review of Original ANDAs, Amendments and Supplements, November 2017
- Draft Guidance for Industry: Information Requests and Discipline Review Letters Under GDUFA, December 2017
- MAPP 5220.5, Issuance of Information Requests and/or Discipline Review Letters for Abbreviated New Drug Applications, December 2017
- Draft Guidance for Industry: Good ANDA Submission Practices, January 2018
- MAPP 5241.3: Good Abbreviated New Drug Application Assessment Practices, January 2018
- Final Guidance for Industry: ANDA Submissions – Amendments to Abbreviated New Drug Applications Under GDUFA, July 2018
- MAPP 5240.5 Rev. 1: ANDA Suitability Petitions, August 2018
- Final Guidance for Industry: ANDA Submissions – Content and Format of ANDAs, September 2018
- MAPP 5014.1: Understanding CDER's Risk-Based Site Selection Model, September 2018

Pre-ANDA Program Goals – FY 2018 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 facilitate the path to market approval.

One example of FDA's commitment to this program has been its product-specific guidances and recommendations for regulatory submissions (e.g., ANDAs, pre-ANDA meeting requests, CCs). FDA developed and published 208 new and revised draft product-specific guidances in FY 2018. The table below shows the product-specific guidance breakdown for complex and non-complex drug products.

	Complex drug products	Non-complex drug products
Number of new product-specific guidances	56	80
Number of revised draft product-specific guidances	20	52
TOTAL	76	132

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

Since FY 2013, FDA has awarded 135 research contracts and grants. A complete list of FY 2013 through FY 2018 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
2018	24	16

Significant FY 2018 Research Accomplishments

In addition to serving as the scientific basis for the development of product-specific guidances and specific pre-ANDA communications, research outcomes are published in the peer-reviewed scientific literature, presented and discussed at major medical and scientific meetings, and contribute to general guidance development. GDUFA research includes the following research programs, each highlighted with a key FY 2018 outcome.

FDA's pre-ANDA work through intramural and extramural research and guidance development has resulted in studies and publications that are available to aid generic drug product applicants. FDA's own research facilitates the path towards generic drug product development

by establishing safety, efficacy, and quality standards to help industry bring those products to the public.

- Ophthalmic Drug Products

  In FY 2018, three peer-reviewed publications on cyclosporine ophthalmic emulsion were published in scientific journals. One study evaluated how changes in excipients of cyclosporine emulsions can affect the globule size measured using five different analytical techniques.[26] In another study, a size-based separation and characterization method (asymmetric flow field flow fractionation) was used to investigate the polydisperse globule size distribution of cyclosporine emulsion formulations.[27] To statistically evaluate polydisperse globule size distributions of cyclosporine emulsion, a statistical approach (Earth Mover's Distance) was proposed as a new metric for comparisons between generic and brand products.[28] This work provided understanding of the various analytical and statistical methods that could be used for assessment of generic versions of ophthalmic emulsions.

- Complex Mixtures and Peptides

  In October 2017, FDA published the draft guidance entitled *ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin*.[29] This guidance discusses when an application for a chemically manufactured peptide drug product that refers to a previously approved peptide drug product that is manufactured by a cell-based recombinant DNA (rDNA) manufacturing process should be submitted as an ANDA under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) rather than as a new drug application (NDA). Before the draft guidance, there were no recommendations for an ANDA submission pathway for the five peptides covered in the guidance.

- Long-Acting Injectables

  Poly(lactic-co-glycolic acid) or PLGA is biodegradable polymer that is widely used in long-acting injectable products. It is the product component that controls the drug release rate. In collaboration with researchers at Purdue University, FDA scientists published an article *Beyond Q1/Q2: The Impact of Manufacturing Conditions and Test Methods on Drug Release From PLGA-Based Microparticle Depot Formulations*[30] that provides advice on the use and characterization of PLGA to generic drug developers. There are currently no approved generic drug products in this product category, and this research will help potential applicants move PLGA-based products through the development process.

[26] Int J Pharm. 2018 Oct 25;550(1-2):229-239.
[27] Int J Pharm. 2018 Mar 1;538(1-2):215-222.
[28] AAPS J. 2018 Apr 12;20(3):62.
[29] www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM578365.pdf
[30] J Pharm Sci. 2018 Jan;107(1):353-361.

- Complex Injectables and Nanomaterials

  FDA scientists published a set of four papers[31] that described detailed comparisons of the approved generic Sodium Ferric Gluconate Complex with the brand product. These publications demonstrated no significant differences in physicochemical characterization, in vitro cellular uptake, and biodistribution between brand and generic drug products. This research demonstrates the level of equivalence and sameness of complex generic drug products that have been approved by FDA's generic drug program and strengthens confidence in future complex generic drug approvals.

- Orally Inhaled and Nasal Drug Products

  FDA completed a pharmacokinetic study that compared different formulations of fluticasone propionate to help us develop new bioequivalence approaches for inhaled corticosteroids. These results are being analyzed and prepared for publication. FDA scientists also published work that will aid generic drug developers in identifying critical formulation attributes for Metered Dose Inhalers[32] and using realistic in vitro models of lung deposition[33] to streamline and expedite development of generic versions of inhaled drug products.

- Topical Dermatological Drug Products

  FDA issued 13 product-specific guidances that recommend in vitro bioequivalence approaches for topical products. These guidances were the result of research that began in FY 2013 on the characterization of topical semi-solid formulations and the linking of that data to its clinical impact. We anticipate this research will help accelerate the development of generic versions of these complex products.

- Physiologically-Based Absorption and Pharmacokinetic Models

  FDA scientists collaborated with external experts to develop, evaluate, and improve physiologically-based models for the most challenging routes of delivery for generic drug development: ophthalmic,[34] inhalation,[35] and dermal.[36] These models aid generic drug development for these routes and help FDA evaluate new bioequivalence approaches for these complex routes of delivery.

- Quantitative Clinical Pharmacology

  Quantitative Clinical Pharmacology was highlighted in the FDA public workshop titled "Leveraging Quantitative Methods and Modeling to Modernize Generic Drug Development and Review" (October 2-3, 2017). The published workshop

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[31] Nanomaterials (Basel). 2017 Dec 28;8(1) Nanomaterials (Basel). 2018 Feb 11;8(2) Nanomaterials (Basel). 2018 Jan 5;8(1) Nanomaterials (Basel). 2017 Dec 15;7(12).
[32] AAPS PharmSciTech. 2018 Jul;19(5):2335-2345
[33] J Aerosol Med Pulm Drug Deliv. 2018
[34] Comput Biol Med. 2018 Jan 1; 92:139-146.
[35] Int J Numer Method Biomed Eng. 2018 May;34(5): e2955
[36] https://www.certara.com/2018/03/02/skin-in-the-game-mechanistic-modeling-of-dermal-drug-absorption/?ap%5B0%5D=PBPK

report[37] highlights how advanced modeling approaches can be applied to increase the efficiency of generic drug development and regulatory decision making.

- Oral Absorption Models and Bioequivalence

  Through a collaboration with the University of Michigan, a series of publications on predictive dissolution of drugs in the human gastrointestinal tract were published. In one study, a mathematical model describing the gastric emptying in the fasted state was explored.[38] An in vitro-in silico-in vivo approach to evaluate the in vivo performance of four different oral formulations of posaconazole was also published.[39] These predictive methods can help evaluate formulation performance in terms of oral bioavailability prior to conducting clinical trials. A clinical study was also conducted to evaluate the in vivo drug dissolution and systemic absorption of ibuprofen by direct sampling of stomach and small intestinal luminal content.[40,41] As limited data is available on in vivo drug dissolution in the gastrointestinal tract, this study provided data that can better support mechanistic absorption model development with the potential to reduce the number of clinical studies needed during generic drug development thus helping to expedite the approval process.

- Generic Drug Substitution

  Researchers funded by FDA grants completed subject dosing for two studies related to generic drug substitution in patients. One evaluated bioequivalence between generic and brand name bupropion HCl modified-release products with different release patterns at a steady state in patients with depression.[42] The second was a pharmacokinetics/pharmacodynamics (PK/PD) classroom study in pediatric ADHD patients (6-12 years of age) to link the PK profiles to the time-course of PD activity of methylphenidate extended release products. A unique feature of this study was that PK sampling was performed through dried blood spots (rather than traditional phlebotomy) because of the subject population and to reduce interference between PK and PD measures (i.e., intravenous blood draws could impact subject behavior in the classroom). The results of these studies are being analyzed and prepared for publication.[43]

- Abuse-deterrent Opioid Drug Products

  FDA posted the final guidance on *General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products* (November 2017).[44] FDA also completed an in vivo nasal pharmacokinetic study on milled oxycodone hydrochloride extended-release tablets, which illustrates how applicants can

[37] Clin Pharmacol Ther. 2018 Jul;104(1):27-30
[38] Mol Pharm. 2018 Jun 4;15(6):2107-2115
[39] Eur J Pharm Sci. 2018 Mar 30; 115:258-269.
[40] Mol Pharm. 2017 Dec 4;14(12):4295-4304.
[41] Mol Pharm. 2017 Dec 4;14(12):4281-4294.
[42] https://clinicaltrials.gov/ct2/show/NCT02209597
[43] https://clinicaltrials.gov/ct2/show/NCT02536105
[44] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM492172.pdf

conduct the in vivo study recommended in the guidance. The results are being prepared for publication and will aid generic drug developers in the successful implementation of this guidance.

- Data Analytics

  FDA developed equivalence methods for comparing the complex particle size distribution (PSD) profiles (e.g., multiple peaks) between brand and generic products.[45] Previous PSD analysis methods (e.g., D50/SPAN) are sufficient to evaluate monomodal PSD profiles (i.e., one peak), but not suitable for analyzing complex PSD profiles. The new approach employs a statistical distribution comparing algorithm, Earth Mover's Distance, to assess the difference between the whole PSD profiles, and then applies the population bioequivalence method to draw statistical conclusions. This approach has been included in the product-specific guidance for cyclosporine emulsion and barium sulfate suspension, and it aids generic drug developers in demonstrating that brand and generic products have the same particle size distribution.

- Drug-Device Combinations

  FDA research established the general utility of an in vitro permeation test methodology to compare heat effects between prospective generic and brand transdermal systems.[46] This work can be used by generic drug developers to design transdermal systems that perform the same as the brand product. It can also be used by FDA to compare brand and generic transdermal products without using in vivo studies, which can increase the efficiency of generic drug development.

FY 2019 Generic Drug Research Priorities

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

On May 24, 2018, FDA held the FY 2018 "Generic Drug Regulatory Science Initiatives Public Workshop," which provided an overview of the status of the human generic drug regulatory science program and an opportunity for public input in developing the FY 2019 research priorities. Information obtained during the public workshop and other inputs, e.g., comments to the public docket, were considered in developing the FY 2019 Regulatory Science Plan.[47]

[45] AAPS J. 2018 Apr 12;20(3):62
[46] J Control Release. 2018 Jan 28;270:76-88
[47] The list of the FY 2019 research initiatives can be found at: www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/UCM626329.pdf

The lists of research initiatives for earlier fiscal years are also available on FDA's website.[48,49]

The FY 2019 human generic drug regulatory science priorities identified were grouped into the following four topic areas:

- Topic 1: Complex active ingredients, formulations, or dosage forms
- Topic 2: Complex routes of delivery
- Topic 3: Complex drug-device combinations
- Topic 4: Tools and methodologies for bioequivalence and substitutability evaluation

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

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

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

Drug Safety and Inspections Performance

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

This section satisfies the annual reporting requirement created by the GDUFA II Commitment Letter for FY 2018 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:

> *g) Number of inspections conducted by domestic or foreign establishment location and inspection type (PAI* [Pre-Approval Inspection]*, GMP* [Good Manufacturing Practice]*, BE* [Bioequivalence] *clinical and BE analytical) and facility type (FDF, API* [Active Pharmaceutical Ingredients]*, etc.),*
>
> *h) Median time from beginning of inspection to* [FDA Form] *483 issuance,*
>
> *i) Median time from 483 issuance to Warning Letter, Import Alert and Regulatory Meeting for inspections with final classification of OAI* [Official Action Indicated] *(or equivalent),* [and]
>
> *j) Median time from date of Warning Letter, Import Alert and Regulatory Meeting to resolution of OAI status (or equivalent).*

FDA interprets the Commitment Letter:

- to be 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 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 only counts that as one inspection.

- Form FDA 483,[50] *Inspectional Observations*, is the list of observations of objectionable conditions issued by FDA investigators to the inspected facility's management at the conclusion of an inspection. Inspections not resulting in issuance of a Form FDA 483 are excluded from paragraphs "h," "I," and "j" of the Commitment Letter (see Section VI, Part C).

[50] More information about Form FDA 483 can be found at: www.fda.gov/ICECI/Inspections/ucm256377.htm

Further, most facilities receiving a 483 are classified as Voluntary Action Indicated (VAI) and no compliance action (Warning Letter, Import Alert, or Regulatory Meeting) is taken.

- PAI of only ANDA applications are counted in this report. If there was a PAI of a New Drug Application (NDA) 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.

- FDA conducts other types of inspections of facilities in which a conclusion of non-compliance may result in delay or denial of application approval. Inspections other than PAI 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 Warning Letter (WL), addition to an Import Alert (IA), or the holding of a Regulatory Meeting, could follow other types of inspections, though not a PAI alone. For that reason, FDA interprets paragraphs "i" and "j" of the Commitment Letter to apply to inspections other than PAI.

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

- BE inspections only have Untitled Letters (UL) issued after an OAI inspection. An 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, we are not including in this report information about events that occurred before FY 2018 except as described below. Accordingly:

- For subparagraphs "g" and "h" of the Commitment Letter we include an inspection for which the inspection ended in the reporting FY, even if the inspection started before the reporting FY. Multiple products/applications can be covered in one inspection assignment, and we count these as one inspection.

- For subparagraph "i" of the Commitment Letter, we will report on Warning Letters, Import Alerts, and Regulatory Meetings that were issued or held in the reporting FY, even if they are based on an inspection for which the 483 was issued before the reporting FY, provided it was issued during the period covered by the GDUFA II Commitment Letter.

- For subparagraph "j" of the Commitment Letter, we will report on resolutions of Warning Letters, Import Alerts, and Regulatory Meetings when the resolutions occurred in the reporting FY even if the Warning Letters, Import Alerts, and Regulatory Meetings were issued or held prior to the reporting FY, provided they were issued or held in or after FY18, the effective starting year for GDUFA II reporting.

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

Number of inspections conducted by type

	Location			
Inspection Type	**Domestic**	**Foreign**	**Total***	**Number Issued 483**
PAI (API)**	3	46	49	33
PAI (API/FDF)**	3	16	19	10
PAI (FDF)**	65	77	142	95
PAI (Other)**	17	15	32	16
CGMP (API)	24	211	235	135
CGMP (API/FDF)	24	43	67	40
CGMP (FDF)	126	109	235	162
CGMP (Other)	62	33	95	52
BE**^	25	36	61	12
BE Clinical**^^	31	28	59	11
BE Analytical**^^	6	22	28	7

*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 BE Inspection Type includes only those Clinical and Analytical inspections assigned in FY17 but closed in FY18.
^^ Bioequivalence inspection tracking was subcategorized into BE Analytical and BE Clinical for assignments issued in FY18.

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

Median time from beginning of inspection to 483 issuance

User Fee Program	FY 2018 Median Time (Calendar Days)
GDUFA	5

The following table shows the median time (calendar days) between the issuance of a 483 and the issuance of a Warning Letter, Import Alert, and date of a Regulatory Meeting. This includes WLs, IAs, and Regulatory Meetings that were issued or held in the reporting FY, even if they are based on an inspection for which the 483 was issued before the reporting FY. The same facility may receive multiple compliance actions, for example a Warning Letter and an Import Alert, following issuance of a 483. Most facilities receiving a 483 are classified VAI and no WL, IA, or Regulatory Meeting is issued or held.

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

User Fee Program	FY 2018 Median Time FDA 483 to WL	FY 2018 Median Time FDA 483 to IA	FY 2018 Median Time FDA 483 to Reg. Meeting
GDUFA	193	105	158

The following table shows the median time (calendar days) between the issuance or holding of a WL, IA, and Regulatory Meeting and OAI resolution. OAI resolution includes the time to remediate CGMP issues at a site classified as OAI and the time for FDA to re-inspect the facility to confirm whether adequate remediation has, indeed, taken place. The compliance action is considered "resolved" when the firm has addressed the violations or deviations sufficiently 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 FY. The same facility may receive more than one compliance action, for example a WL and an IA, following issuance of a 483.

Median time from date of Warning Letters, Import Alert and Regulatory Meeting to resolution of OAI status

User Fee Program	FY 2018 Median Time OAI Finalized to Resolution	FY 2018 Median Time WL to OAI Resolution	FY 2018 Median Time IA to OAI Resolution	FY 2018 Median Time Reg. Meeting to OAI Resolution
GDUFA	N/A	N/A	N/A	N/A

There were no facilities issued a WL, IA, and Regulatory Meeting with OAI resolution both occurring in or after FY 2018, the beginning of the GDUFA II reporting period. Resolution includes the firm addressing the GMP violations or deviations that resulted in the OAI outcome, and re-inspection and classification of the site as VAI or NAI, if appropriate.

Significant remediation efforts by the firm to resolve the CGMP issues at a site classified as OAI and subsequent reinspection by the 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 to not remediate, or never adequately remediate, and violations observed at their facilities and compliance actions remain open indefinitely.

Inspection Efficiency Enhancements

The Agency has implemented various changes, continues to improve how FDA conducts inspections to verify pharmaceutical quality, and has improved transparency and timeliness in determining regulatory outcomes from inspections.[51]

In FDASIA, 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

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

determining that the foreign government has the capability to conduct inspections in accordance with the FD&C Act (section 809). FDA is currently implementing a mutual recognition agreement with the European Union (EU), which allows both parties to rely on our respective surveillance inspections in lieu of performing repetitive inspections of the same facilities. FDA and the EU are now relying on inspections in those countries found capable on a rolling basis, and all capability determinations should be completed by July 2019.

Outreach and Facility Assessment

FDA completed multiple commitments under GDUFA II to provide greater transparency regarding prioritization and scheduling of inspections and regarding communicating information following inspections. These efforts include updating FDA's publicly available inspection classifications database,[52] 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.

- 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 bioequivalence/bioavailability studies. The database is updated every 30 days. Previously, the database was updated every 180 days and did not include inspection classifications of sites conducting clinical bioequivalence/bioavailability studies. The database has also been updated to build on our progress implementing the Mutual Recognition Agreement[53] with the EU, and now supports inclusion of facility status based on classification of inspection reports from foreign regulatory authorities.

- Under GDUFA II, FDA committed to updating the inspection classifications database by January 1, 2019, and to continue to update it every 30 days. Due to the interest in making this information available to drug manufacturers, applicants, foreign regulators, and the public, FDA worked diligently to complete the commitment in advance of that goal. Moreover, FDA's Office of Regulatory Affairs worked with the Agency's product Centers to go beyond the commitment by including available information and updating the database every 30 days for inspections of all FDA-regulated medical products.

- The inspection classifications database also meets, in part, a GDUFA II commitment regarding communications with foreign regulators. Currently, foreign regulatory authorities may contact FDA for information regarding a facility physically located in the United States prior to that facility being allowed to export a product to that country. Under GDUFA II, FDA committed to respond to such requests within 30 days. The Agency has now more formally implemented procedures to meet those commitments, but the database will also facilitate foreign regulators' ability to check the most recent inspection classification on their own.

- In addition, FDA has also published MAPP 5014.1, "Understanding CDER's Risk-Based Site Selection Model," which is published at FDA's website. Under GDUFA II, FDA committed to explaining the Agency's risk-based site selection model for human pharmaceutical manufacturing establishments. This MAPP outlines the policies and procedures for the Site

[52] https://www.fda.gov/ICECI/Inspections/ucm222557.htm
[53] https://www.fda.gov/InternationalPrograms/Agreements/ucm598735.htm

Selection Model (SSM) used by CDER staff to prioritize manufacturing sites for routine CGMP surveillance inspections. The MAPP outlines the risk factors that are considered for sites included in the SSM as well as the process for continual improvement of the model.

- A presentation on the above MAPP and the inspection classifications database was given at the most recent Pharmaceutical Inspection Co-operation Scheme (PIC/S) Annual Seminar in Chicago, IL in September 2018. PIC/S, comprised of 52 participating authorities from around the world, focuses on the international development, implementation, and maintenance of harmonized CGMP standards and quality systems of inspectorates in the field of pharmaceutical products.

- FDA has also implemented commitments concerning communication of facility inspection information to facility owners. In 2017, the Agency instituted a Concept of Operations agreement[54] and began issuing letters to communicate inspection classification information to facility owners within 90 days of the close of a surveillance inspection. FDA is now consistently issuing these letters for surveillance inspections of non-compounding drug facilities. In addition, FDA has established procedures so that when application-related inspections (i.e., pre-approval inspections) of facilities or sites associated with ANDAs, PASs, or Type II DMFs result in identification of issues that could impact approvability of the application or supplement, the applicant will be notified through an IR, DRL, or CRL.

Completing these commitments provides industry and stakeholders with more transparent and timely information regarding inspections, which can help companies make more informed marketplace choices as well as more quickly resolve issues that could impact application approvals.

[54] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm576309.htm

GDUFA II - Enhanced Accountability and Reporting

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

Resource Management Planning and Modernized Time Reporting

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

Activity	Due Date/Deadline	Status
FDA will develop and publish a resource management planning and modernized time reporting implementation plan	No later than the fourth quarter of FY 2018	FDA published the implementation plan on March 30, 2018
FDA will contract with an independent third party to obtain an evaluation of options and recommendations for a methodology to accurately assess changes in resources needs of the human generic drug review program and how it monitors and reports on those needs	The report should be published no later than the end of FY 2020 for public comment	In Progress
FDA will implement methodologies for assessing resource needs of the program and tracking resource utilization across the program elements	Following the report review and comments	

Financial Transparency and Efficiency

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

Activity	Due Date/Deadline	Status
FDA will contract with an independent third party to obtain an evaluation of how the GDUFA program is resourced and how those resources are utilized; the evaluation will also recommend improvements to the process		In Progress
FDA will use the results of the evaluation to create an ongoing financial reporting mechanism to enhance the transparency of GDUFA program resource utilization		In Progress
FDA will publish a GDUFA 5-year financial plan	No later than the 2nd quarter of FY 2018	FDA published the Five-Year Financial Plan
FDA will publish updates to the GDUFA -year financial plan	No later than the 2nd quarter of each subsequent fiscal year	

Performance Reporting

In the GDUFA II Commitment Letter, FDA committed to publish monthly and quarterly performance metrics on its website. These metrics can be found on the FDA website at: www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/ucm375079.htm (monthly) and www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm600678.htm (quarterly).

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

The following table summarizes FDA's GDUFA II commitment to promote accountability and transparency by providing the mean and median approval times for generic drug reviews for the FY 2018 receipt cohort. These metrics only include applications approved or tentatively approved at the time this report was prepared. In future congressional reports, 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 congressional reports.

GDUFA II	FY 2018
Receipt Cohort (Preliminary Data)	
Mean Approval Time (days)	294
Median Approval Time (days)	296
Mean Tentative Approval Time (days)	313
Median Tentative Approval Time (days)	313
Mean Number of ANDA Review Cycles to Approval	1
Median Number of ANDA Review Cycles to Approval	1
Mean Number of ANDA Review Cycles to Tentative Approval	1
Median Number of ANDA Review Cycles to Tentative Approval	1

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

GDUFA II	FY 2018
Application Receipt	
Number of Applications Received	844
Number of Applications Refused to Receive	79
Average Time to Receipt Decision	49
ANDA Review	
Number of ANDA Applications Received by FDA for Standard Review	463
Number of ANDA Applications Received by FDA for Priority Review	381
Percentage of ANDA proprietary name requests reviewed within 180 days of receipt	97%
Petitions	
Number of suitability petitions pending a substantive response for more than 270 days from the date of receipt	136
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
DMF	
Number of DMF First Adequate Letters issued status (or equivalent)	259
Email Exchanges	
Number of email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in first cycle DMF deficiency letters	56
Number of email exchanges requested and conducted in lieu of teleconferences to clarify deficiencies in follow-up cycle DMF deficiency letters	10

Management Initiative	Performance Area	FY 2018
When requested by the ANDA applicant within 10 calendar days of FDA issuing CRL, FDA will schedule a teleconference to provide clarification concerning deficiencies identified in the CRL.[55]	Teleconferences Requested	70
	Teleconferences Granted	53
	Teleconferences Denied	17
	Teleconferences Conducted	53
When requested by the ANDA applicant, FDA will schedule a teleconference to clarify issues and answer question on reclassifying a major amendment or standard review status	Teleconferences Requested	30
	Teleconferences Granted	24
	Teleconferences Denied	0
	Teleconferences Conducted	24
FDA will offer to hold a mid-review cycle teleconference with an applicant if a product development or pre-submission meeting has been held.[56]	Teleconferences Offered	1
	Meetings Scheduled	1
	Meetings Conducted	0

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

[56] The Commitment Letter specifies *requested*, *granted*, *denied*, and *conducted*, but these terms do not neatly apply to mid-review cycle meetings. The more applicable terms *offered*, *scheduled*, and *conducted* are used instead.

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Appendices

Appendix A: Definitions of Key Terms

A. Act on an Application means that FDA will either issue a complete response letter (CRL), an approval letter, a tentative approval (TA) letter, or a refuse-to-receive (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 – This GDUFA Performance Report covers FY 2017, the final year of GDUFA I and FY 2018, the first year of GDUFA II. 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 a major or minor, and whether or not a preapproval inspection is needed.

GDUFA II – 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 the FDA 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 which are contained in Appendix B of the July 2018 guidance. See https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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

F. Complete response letter (CRL) – refers to a written communication to an applicant or DMF holder from FDA usually describing all of the deficiencies that the Agency has identified in an

abbreviated application (including pending amendments) or a DMF that must be satisfactorily addressed before the ANDA can be approved. Complete response letters will reflect a complete review which includes an application-related facilities assessment and will require a complete response from industry to restart the clock. Refer to 21 CFR 314.110 for additional details. When a citizen petition may impact the approvability of the ANDA, FDA will strive to address, where possible, valid issues raised in a relevant citizen petition in the complete response letter. If a citizen petition raises an issue that would delay only part of a complete response, a response that addresses all other issues will be considered a complete response.

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 – means:

1. Controlled correspondence involving evaluation of clinical content,

2. Bioequivalence protocols for Reference Listed Drugs with Risk Evaluation and Mitigation Strategies (REMS) Elements to Assure Safe Use (ETASU), 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 a 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 guidance for industry Controlled Correspondence Related to Generic Drug Development.[57] CC does not include Citizen Petitions, petitions for reconsideration, or requests for stay.

K. Delaying Amendment – GDUFA I Commitment Letter - refers to amendments to an ANDA from the ANDA applicant to address actions by a third party that would cause delay or impede application review or approval timing and that were not or may not have been initially recognized

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

by FDA as necessary when the application was first submitted. FDA's Office of Generic Drugs shall have broad discretion to determine what constitutes a delaying event caused by actions generally outside of the applicants control taking into account facts and information supplied by the ANDA applicant.

L. 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.

M. 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 active pharmaceutical ingredient or a finished dosage form, 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.

N. 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

O. 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.

P. Mid-review-cycle meeting –after the last key discipline has issued its IR and/or DRL, for ANDAs that were the subject of prior Product Development Meetings or pre-submission meetings, CDER will schedule a teleconference meeting with the applicant to discuss current concerns with the application and next steps.

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

R. 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.

S. 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 abbreviated new drug application 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.[58]

[58] Per section 744A(11) of the FD&C Act.

T. 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 Manual of Policy and Procedures (MAPP) 5240.3, *Prioritization of the Review of Original ANDAs, Amendments and Supplements*, as revised (the CDER Prioritization MAPP).

U. 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.

V. Review Status Update – means a response from the 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. The RPM will advise the Authorized Representative that the update is preliminary only, based on the RPM's interpretation of the submission, and subject to change at any time.

W. Standard controlled correspondence (CC) – means controlled correspondence

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

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

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

Y. Submission refers to an ANDA, an amendment to an ANDA, a PAS to an ANDA, or an amendment to a PAS.

Z. Submission date means the date that a generic drug submission or Type II DMF is deemed to be "submitted" pursuant to the applicable statute Section 744B(a)(6) of the FD&C Act states that a generic drug submission or Type II DMF is deemed to be "submitted" if it is submitted via a 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, April 2018. See https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

AA. Target Action Date (TAD) - Under GDUFA I, FDA's aspirational deadline for action on a pre-GDUFA I Year 3 original ANDA and/or a complete response amendment or equivalent IR to an original ANDA. GDUFA I TADs become GDUFA II goal dates on enactment of GDUFA II.

BB. Tentative Approval (TA) Letter - If a generic drug product is ready for approval but cannot be approved due to a patent or exclusivity related to the reference listed drug product, FDA issues a TA letter to the applicant, and the TA letter details the basis for the TA. FDA will not issue final approval of the generic drug product until all patent or exclusivity issues have been resolved or, in some cases, until a 30-month stay associated with patent litigation has expired. A TA does not allow the applicant to market the generic drug product.

CC. Type II API Drug Master File (DMF) is defined in section 744A(13) as a submission of information to the FDA concerning the manufacture of a pharmaceutical active ingredient by a person that intends to authorize the FDA to reference the information to support approval of a generic drug submission without the submitter having to disclose the information to the generic drug submission applicant.

Appendix B: FY 2019 Generic Drug Regulatory Science Priorities Topic Areas

Under GDUFA, FDA committed to develop an annual list of regulatory science priorities for generic drugs. FDA organized its FY 2019 priorities into the following topic areas:

A - Complex active ingredients, formulations, or dosage forms

1. Improve advanced analytics for characterization of chemical compositions, molecular structures and distributions in complex active ingredients
2. Improve particle size, shape and surface characterization to support 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 bioequivalence (BE) methods for long-acting injectables including the identification of the critical quality attributes (CQA) for these products
5. Develop better methods for evaluating abuse deterrence of generic solid oral opioid products, including in vitro alternatives to in vivo nasal studies

B - Complex routes of delivery

1. Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)
2. Expand characterization-based bioequivalence (BE) methods across all topical dermatological products
3. Expand characterization-based BE methods across all ophthalmic products
4. Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) comparative clinical endpoint BE studies for inhaled corticosteroids
5. Develop alternatives to comparative clinical endpoint BE studies for locally-acting nasal products that are more predictive of and sensitive to differences in local delivery

C - Complex drug-device combinations

1. Evaluate the impact of identified differences in the user-interface from the RLD on the substitutability of complex generic drug-device combination products

D - Tools and methodologies for BE and substitutability evaluation

1. Improve quantitative pharmacology and BE trial simulation to optimize design of BE studies for complex generic drug products
2. Integrate predictive dissolution, PBPK and Pharmacokinetic/Pharmacodynamic (PK/PD) models establishing generic drug bioequivalence standards
3. Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System (BCS) of Class 3 biowaivers to non-Q2 (quantitatively inequivalent) formulations
4. Develop methods that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution/utilization patterns, drug safety data and drug quality data) to support regulatory decisions and improve post-market surveillance of generic drug substitution

Appendix C: Analysis of Use of Funds

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

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

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

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

While 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 a substantially complete application 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	Review Goal	Received	Received with Goal in FY 2019	Approved	Tentatively Approved	Complete Response	Missed Goal*	Percent on Time†	Potential Range†
I. Original ANDA Review Goals									
Standard Original ANDA Applications	10 months	469	434	5	3	30	3	96%	14% to 99%
Priority Original ANDA Applications (if applicant meets requirements of a Pre-Submission Facility Correspondence (PFC))	8 months	28	25	0	0	3	0	100%	28% to 100%
Priority Original ANDA Applications (if the applicant does not meet the requirements of a PFC)	10 months	351	286	3	0	63	4	96%	25% to 99%
II. Amendment Review Goals									
Standard Major ANDA Amendments (if preapproval inspection is not required)	8 months	750	543	38	5	179	9	96%	29% to 99%
Standard Major ANDA Amendments (if preapproval inspection is required)	10 months	32	32	0	0	0	0	–	0% to 100%
Priority Major ANDA Amendments (if pre-approval inspection is not required)	6 months	280	201	14	6	70	1	99%	32% to 100%
Priority Major ANDA Amendments (if preapproval inspection is required and applicant meets the requirements of a PFC)	8 months	–	–	–	–	–	–	–	–
Priority Major ANDA Amendments (if preapproval inspection is required and applicant does not meet the requirements of a PFC)	10 months	10	10	0	0	0	0	–	0% to 100%
Standard and Priority Minor ANDA Amendments	3 months	1,233	415	292	99	441	58	93%	64% to 95%

*Missed Goals includes 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 the FDA to include relevant data to determine whether CDER and CBER have met performance enhancement goals identified in the letters described in section 301(b) of GDUFA II (GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (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 GDUFA 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
Issue MAPP setting forth procedures for filing reviewers on communication of minor technical deficiencies.	10/1/2017	Y	9/28/2017	. https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM578093.pdf
Update the Inactive Ingredient Database on an ongoing basis and post quarterly notice of updates made.	Quarterly	Y	Quarterly	https://www.accessdata.fda.gov/scripts/cder/iig/index.Cfm
Conduct a public workshop to solicit input from industry and stakeholders for inclusion in an annual list of GDUFA II Regulatory Science initiatives.	Annually	Y	Public Workshop Held May 24, 2018	https://www.fda.gov/Drugs/NewsEvents/ucm583766.htm
Meetings between FDA and industry GDUFA II regulatory science working group.	Biannually	Y	First Meeting Held April 10, 2018. Second Meeting Held on November 1, 2018	FDA offered to meet with industry for the second time on September 1, 2018. However, based on a mutual agreement the meeting was held in November. FDA met with industry twice and considers this goal to be met.
Notify applicants of certain inspection issues affecting approval of their submission through IRs, DRLs, or CRLs.	May 31, 2018	Y	February 12, 2018	No further comment.
Publish a GDUFA program resource management planning and modernized time reporting implementation plan.	9/30/2018	Y	9/30/2018	No further comment.

Performance Enhancement Goal	Target Goal Date	On Time (Y/N)	Actual Completion Date	Comments
Publish a GDUFA 5-year financial plan.	March 31, 2018	Y	March 29, 2018	FDA posted the plan at https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/UserFeeFiveYearFinancialPlans/UCM603104.pdf.
Post monthly reporting metrics set forth under section VI(C)(1)(a) through (d) of the GDUFA II Commitment Letter.	Monthly	Y	Monthly	FDA posted these monthly metrics at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm375079.htm.
Post quarterly reporting metrics set forth under section VI(C)(2)(a) through (d) of the GDUFA II Commitment Letter.	Quarterly	Y	Quarterly	FDA posted these quarterly metrics at https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm600678.htm.
Post annual reporting metrics set forth under section VI(C)(3)(a) through (p) of the GDUFA II Commitment Letter.	Annual	Y	Annual	Please see the Performance Reporting Section of the FY 2018 GDUFA Performance Report.

C. Common Causes and Trends Impacting Ability to Meet Goals

The following table addresses section 904(c)(1) of FDARA, pertaining to GDUFA, 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.

Cause or Trend	Impact on FDA Ability to Meet Goals
Small number of submissions for the Priority Major PAS Amendments (if Preapproval Inspection is not required) review goal	Some of the submissions that fall under this review goal category and submissions that fall under the other review goal categories received in FY 2018 have associated review time goals that fall within the subsequent fiscal year. At this time, it appears that due to a small number of Priority Major PAS Amendments (if Preapproval Inspection is not required) received (i.e., 8 total), missing the goal for a single submission will result in dropping below the GDUFA metric of 90 percent. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation and a corrective action report for this fiscal year in next year's GDUFA performance report and appropriate appendices.

Appendix D: FY 2018 Corrective Action Report

FY 2018 Corrective Action Report

On August 18, 2017, FDARA (Public Law 115-52) was signed into law. FDARA amends the FD&C Act to revise and extend the user fee programs for drugs, biologics, medical devices, and biosimilar biological products, and for other purposes. Among the provisions of Title IX, section 904 of FDARA, the FDA is required to issue a corrective action report that details FDA's performance in meeting the review and performance enhancement goals identified in section 301(b) of GDUFA II (GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (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.[59]

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 providing this information in an effort to be complete.

This appendix satisfies this reporting requirement.

[59] FD&C Act 744C (21 USC 379j).

Executive Summary

FY 2018 Review Goal Performance

Goal Type	Circumstances and Trends Impacting Ability to Meet Goal Date	Corrective Action Plan
Review Goals	Small number of submissions for the Priority Major PAS Amendments (if Preapproval Inspection is Not Required) review goal	Some of the submissions that fall under this review goal category and many submissions that fall under the other review goal categories received in FY 2018 have associated review time goals that fall within the subsequent fiscal year. At this time, it appears that due to a small number of Priority Major PAS Amendments (if Preapproval Inspection is not required) received (i.e., eight total), missing the goal for a single submission will result in dropping below the GDUFA metric of 90 percent. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation and a corrective action report for this fiscal year in next year's GDUFA performance report and appropriate appendices.
Review Program Enhancement Goals	Too soon to determine.	Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.
Pre-ANDA Program Goals	Too soon to determine.	Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.
Facilities Goals	Too soon to determine.	Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.
Enhanced Accountability and Reporting Goals	All FY 2018 goals met.	No corrective action plan needed.

FY 2018 Performance Enhancement Goal Performance

Goal Type	Circumstances and Trends Impacting Ability to Meet Goal Date	Corrective Action Plan
Policy Documents	All FY 2018 goals met.	No corrective action plan needed.
Public Meetings and Workshops	All FY 2018 goals met.	No corrective action plan needed.
Program and Process Implementation	All FY 2018 goals met.	No corrective action plan needed.
Website Publishing	All FY 2018 goals met.	No corrective action plan needed.

GDUFA Review Goals

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

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

I. FY 2018 Review Goal Performance

A. Summary of Performance: *At this time, it appears that due to the small number of Priority Major PAS Amendments (if Preapproval Inspection is not required) received (i.e., eight total), missing the goal for a single submission will result in dropping below the GDUFA metric of 90 percent. As of September 30, 2018, this particular cohort has three completed actions and five still pending with goal dates that fall within FY 2019. One of the three completed actions during FY 2018 occurred after the goal date; therefore, the greatest potential for meeting this review time goal metric is 88%.*

B. Justification: *Because FDA cannot evaluate the entire performance for FY 2018 it is too soon to determine an appropriate justification.*

C. FY 2019 Corrective Actions: *Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full corrective action for this fiscal year in next year's report.*

II. FY 2018 Review Program Enhancement Goals Performance

A. ***Summary of Performance:*** *Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.*

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

C. ***FY 2019 Corrective Actions:*** *Too soon to determine if a corrective action is needed.*

III. FY 2018 Pre-ANDA Goals Performance

A. ***Summary of Performance:*** *Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate*

the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.

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

C. ***FY 2019 Corrective Actions:*** *Too soon to determine if a corrective action is needed.*

IV. FY 2018 Facilities Goals Performance

A. ***Summary of Performance:*** *Some submissions received in FY 2018 have associated review goals that fall within the subsequent fiscal year. Because FDA cannot evaluate the entire performance for FY 2018 review time goals yet, FDA will provide a full evaluation next year.*

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

C. ***FY 2019 Corrective Actions:*** *Too soon to determine if a corrective action is needed.*

V. FY 2018 Enhanced Accountability and Reporting Goals Performance

A. ***Summary of Performance:*** *All FY 2018 goals met.*

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

C. ***FY 2019 Corrective Actions:*** *No corrective action needed.*

GDUFA Performance Enhancement Goals

The following section addresses section 904(c)(1)(c)(2) of FDARA (section 744C(c)(2) of the FD&C Act), which requires the FDA to provide a justification for missed performance enhancement goals, and a description of the circumstances and any trends that impacted FDA's ability to meet performance enhancement goals during FY 2018.

This section presents non-review performance goals cited in the GDUFA II Commitment Letter with required completion dates in FY 2018. 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 2019 through FY 2022 will be covered in subsequent corrective action reports.

I. Policy Documents

A. ***Summary of Performance:*** *All FY 2018 goals met.*

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

C. ***FY 2019 Corrective Actions:*** *No corrective action needed.*

II. Public Meetings and Workshops

A. ***Summary of Performance:*** *All FY 2018 goals met.*

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

C. ***FY 2019 Corrective Actions:*** *No corrective action needed.*

III. Program and Process Implementation

A. ***Summary of Performance:*** *All FY 2018 goals met.*

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

C. ***FY 2019 Corrective Actions:*** *No corrective action needed.*

IV. Website Publishing

A. ***Summary of Performance:*** *All FY 2018 goals met.*

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

C. ***FY 2019 Corrective Actions:*** *No corrective action needed.*

Department of Health and Human Services
Food and Drug Administration

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

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