



Office of Generic Drugs 2023 Annual Report

Ensuring high-quality, safe, and effective generic
drugs are available to the American public



February 2024

Director's Message

Welcome to the ninth Annual Report from the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER) of the U.S. Food and Drug Administration (FDA).

OGD's mission is to ensure high-quality, safe, and effective generic medicines are available to the American public. Generic drugs are generally lower cost than their brand-name equivalent, allowing patients greater access to medicines. The approval of generic drugs often means multiple manufacturers for medicines, which can help stabilize the supply chain and reduce drug shortage risks.

Reauthorization of the Generic Drug User Fee Amendments

Congress enacted the Generic Drug User Fee Amendments (GDUFA) in 2012, and authorized the third iteration of GDUFA (GDUFA III) in October 2022, following negotiations between FDA and industry along with input from public stakeholders. GDUFA aims to ensure patient access to high-quality, safe, and effective generic drugs, and enables FDA and industry to carry out their important work advancing generic drug development and approval.

Enabled by agreements under GDUFA, we conduct, support, and encourage scientific research to promote innovation that continues to lead to the development of new generic drug products for groundbreaking medicines. Ultimately, American patients benefit from our GDUFA-funded programs, since the program activities contribute to timely approvals of generic medicines.

Scientific Research on Generic Drugs

FDA's generic drug science and research program helps ensure regulatory standards, recommendations, and decisions that impact generic drugs are supported by current scientific insights and research tools. Public input helps the FDA generic drug program identify science and research priorities that can expand and accelerate patient access to generic drugs. FDA then advances research in those scientific areas and publishes annual science and research reports describing the corresponding activities and outcomes.

The outcomes from GDUFA-funded research help expand our understanding of drug products, including complex products, and contribute to the development of advanced methods to characterize product quality and performance. These methods may play a critical role in determining how FDA assesses the bioequivalence and quality of complex generic products and can establish the scientific basis for novel and more efficient pathways by which to develop generic products.



Lilun Murphy, M.D.
Director,
Office of Generic Drugs

ANDAs and First Generic Approvals

In 2023, our generic drug approvals, competitive generic therapy approvals, and first generic approvals remained steady. Of note, we approved the first generic naltrexone extended-release injectable suspension (referencing Vivitrol®). This vital medicine addresses two major public health needs affecting millions of individuals in the United States: treating alcohol dependence and preventing opioid dependence relapse. Critical to the approval of this product were research collaborations to establish methods to assess its bioequivalence which uses complex, long-acting, injectable, biodegradable, polymer-microsphere technology.

International Collaboration

As a global leader in generic drug regulation, OGD collaborated with international regulatory authorities to foster the development of uniform, scientifically driven international standards that can help improve the efficiency of generic drug development by, among other things, preventing unnecessary duplication of studies and testing. In 2023, FDA announced the availability of a harmonized draft guidance for generic drugs on bioequivalence for immediate-release solid oral dosage forms. Regulatory convergence activities like this can help regulatory agencies with timely authorization and availability of quality, safe, and effective generic drugs that benefit patients.

Looking to the Future

OGD will continue to focus on matters such as: operational modernization, workforce excellence, communication through conferences and education, direct engagement with companies developing generic drugs, and the meeting of our overall GDUFA program goals. The Office of Generic Drugs 2023 Annual Report provides a comprehensive look at what we accomplished in 2023 and illustrates how the Agency is well-positioned to continue this critical work in 2024.

lilun Murphy, M.D.

Director, Office of Generic Drugs

“To ensure the availability of safe, effective, and high-quality generic medicines, we will continue to provide scientifically sound recommendations on how to submit strong applications, as well as continue to research practical ways to develop more generics.”

lilun Murphy, M.D.

Director,
Office of Generic Drugs

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2023 Generic Drug Program At-A-Glance

FDA's Office of Generic Drugs (OGD) hailed many successes concurrent with the implementation of the reauthorization of the Generic Drug User Fee Amendments (GDUFA III) including:

956

Approved or tentatively approved generic drug applications, known as Abbreviated New Drug Applications (ANDAs).

1,493

Complete response letters issued in 2023 detailing the deficiencies that applicants needed to resolve before FDA could approve an ANDA.

101

Pre-ANDA meeting requests about product development and/or pre-submission issues addressed.

More than 21,000

Stakeholders worldwide participated (in-person or virtually) across 8 public workshops and 3 webinars.

2,157

Total product-specific guidances (PSGs), including those published in 2023 found on the FDA website [here](#).

\$20 million

In funding provided for generic drug science and research projects in 2023.

158

New and revised Product-specific Guidances (PSGs) for industry and other stakeholders.

12

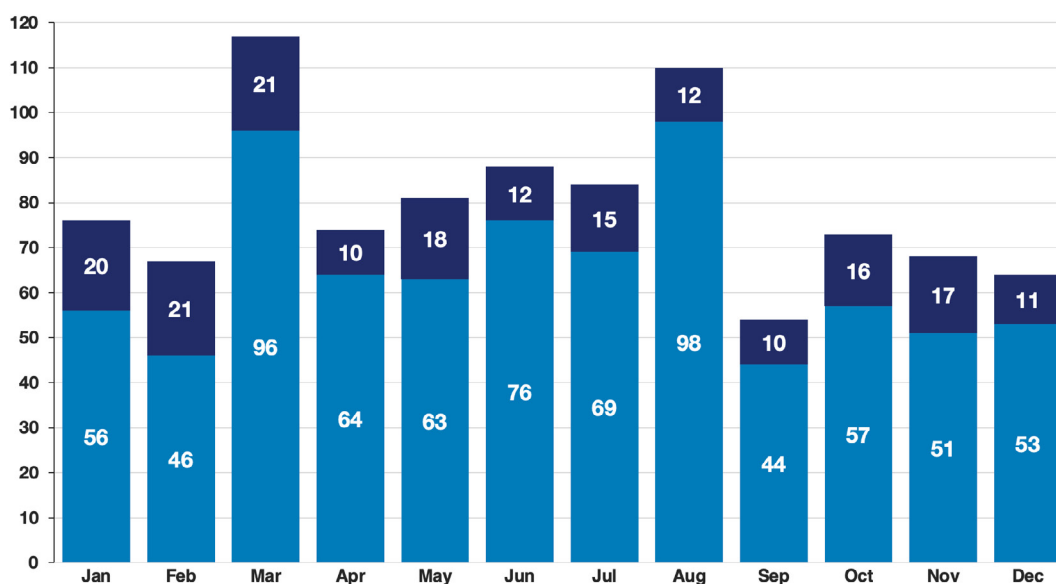
Policy documents published that support generic drug developers by clarifying FDA's scientific and regulatory expectations and that bring greater transparency to the generic drug assessment process, including new GDUFA III enhancements.



Generic Drug Approvals

The impact of generic medicines on the consumer pocketbook is significant – saving consumers billions of dollars over the past decade.¹ In 2023, the generic drug program approved or tentatively approved 956 generic drug applications, known as Abbreviated New Drug Applications (ANDAs).

2023 Generic Drugs Approved and Tentatively* Approved



*A tentative approval does not allow the applicant to market the generic drug product and postpones the final approval until all patent/exclusivity issues have been resolved.

First Generic Drug Approvals

“First generics” provide access where no generic competition previously existed. Because of their importance to public health, FDA prioritizes review of submissions for these products. In 2023, OGD approved 90 first generic medicines.

¹ <https://www.fda.gov/drugs/questions-answers/generic-drugs-questions-answers#q4>

Significant First Generic Drug Approvals in 2023

Generic Name	Brand Name	Indications ²	Date Approved
Obeticholic Acid Tablets	Ocaliva Tablets	Primary biliary cholangitis	5/30/2023
Tiotropium Bromide Inhalation Powder	Spiriva Handihaler	Chronic obstructive pulmonary disease	6/20/2023
Naltrexone for Extended-Release Injectable Suspension	Vivitrol for Extended-Release Injectable Suspension	Prevention of relapse to opioid dependence; treatment of alcohol dependence	7/6/2023
Plerixafor Injection	Mozobil Injection	In combination with granulocyte-colony stimulating factor to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma or multiple myeloma	7/24/2023
Saxagliptin Tablets	Onglyza Tablets	Type 2 diabetes mellitus	7/31/2023
Lisdexamfetamine Dimesylate Capsules and Chewable Tablets	Vyvanse Capsules and Chewable Tablets	Attention Deficit Hyperactivity Disorder; Binge eating disorder	8/25/2023
Palbociclib Tablets	Ibrance Tablets	Breast cancer	8/28/2023
Tofacitinib Oral Solution, 1 mg/mL	Xeljanz Oral Solution	For the treatment of Rheumatoid Arthritis; Psoriatic Arthritis; Ankylosing Spondylitis; Ulcerative Colitis; Polyarticular Course Juvenile Idiopathic Arthritis	9/25/2023
Teriparatide Injection USP, 600 mcg/2.4 mL	Forteo Injection	Osteoporosis	11/16/2023

Spotlight on First Generics: Vyvanse and Tofacitinib

FDA Approved First Generics of Vyvanse

In 2023, FDA approved multiple first generics of lisdexamfetamine dimesylate (referencing Vyvanse®) capsules and chewable tablets for attention deficit hyperactivity disorder (ADHD) in patients 6 years and older and for moderate to severe binge eating disorder (BED) in adults.

FDA Approved First Generic of Tofacitinib

FDA also approved the first generic tofacitinib (referencing Xeljanz®) oral solution for the treatment of moderate to severe rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, ulcerative colitis, and polyarticular course juvenile idiopathic arthritis.

² Due to space limitations, abbreviated indications are listed. For full indication information, please check Drugs@FDA.

Information Requests, Letters, and Controlled Correspondence

OGD communicated with industry through 4,074 information requests (IRs), 2,333 discipline review letters (DRLs), and 1,493 complete response letters (CRLs). These requests and letters identify issues that need to be addressed by applicants before FDA can approve an application. Another important tool used to communicate with industry is controlled correspondence. A controlled correspondence is an inquiry 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 or certain post-approval submission requirements. The opportunity for industry to submit controlled correspondence helps support the submission of higher quality generic drug applications. In 2023, OGD received 3,555 controlled correspondence inquiries.



Generic Drug Regulatory Science Research

How the Generic Drug Program's Research Makes a Difference

The results of OGD's [science and research](#) provide information and tools for industry to develop new generic drug products and for FDA to evaluate the equivalence of the proposed generic drugs. FDA consults with and solicits input from the public, industry, and academia to develop an annual list of [GDUFA Science and Research Initiatives](#) specific to generic drug research.

In 2023, FDA funded approximately \$20 million in science and research projects. FDA awarded funding for 11 new contracts and 9 new grants, as well as 21 ongoing contracts, and 10 ongoing grants. In keeping with FDA's commitment to promote high-quality and clinically relevant science, OGD staff and their external collaborators had 70 peer-reviewed scholarly articles published, presented 172 external talks, and 96 posters at scientific and medical conferences worldwide.

Center for Research on Complex Generics

During 2023, the GDUFA-funded [Center for Research on Complex Generics](#) (CRCG) expanded its scope of activities to enhance research collaborations between FDA, academic institutions, and the generic industry, with the goal of increasing patient access to generic products. These efforts included the formation of the first CRCG Expert Committee, with representatives from the generic drug industry, academia, and government, focused on test methods for transdermal products, an FY 2023 GDUFA priority research area. The CRCG Expert Committee collaborated to design the specific research needed in this area and will continue to guide the conduct of the research.

This direct involvement of generic industry experts in the design and conduct of GDUFA-funded research leverages industry knowledge and perspectives, helping to ensure that the methods fostered are efficient for generic product developers to use, and thereby further facilitate patient access to these complex generics. The CRCG also solicited detailed feedback on scientific and technical challenges impacting the development and assessment of specific generic products. The CRCG and individual generic product developers and other generic industry stakeholders discussed this feedback during multiple meetings, as well as during public workshops hosted by the FDA and the CRCG. The CRCG's detailed insights ensured that GDUFA-funded research focused on the most pressing scientific challenges, and that the research was suitably designed to help product developers effectively develop complex generics.

A New Meeting Pilot for Industry

In 2023, the generic drug program launched a pilot that offers new meeting opportunities to prospective generic drug applicants who are using Model-Integrated Evidence (MIE) approaches for bioequivalence (BE) establishment in their ANDAs.

MIE approaches combine data from in vivo or in vitro studies with scientifically sound mechanistic models, to provide more efficient ways of demonstrating BE in some of the most complex situations facing the generic drug program. As these approaches are novel, success in using them requires early (i.e., during product development) and focused interactions with FDA.

Under the MIE Pilot Program, a meeting may be granted if it pertains to:

- innovative MIE-focused approaches for BE establishment that cannot be effectively addressed under the existing GDUFA scientific meetings,
- non-complex products with complex approaches/modeling that are not in scope of the existing GDUFA scientific meetings, and
- novel data analytics tools and approaches (e.g., machine learning and artificial intelligence) for BE establishment and assessment

Overall, the pilot program serves as a specialized regulatory platform for industry to explore the proposed MIE approaches, obtain FDA's advice on their feasibility and advancement, and address relevant scientific and technical questions. It allows a more intensive focus on model development than the generic drug program's existing GDUFA.

GDUFA Research Program Bridges Knowledge Gaps in Generic Drug Development

Developing innovative methodologies and more efficient tools to help establish drug equivalence standards ultimately supports the development of safe, effective, and high-quality generic drug products, including complex generics. To enhance patient access to complex generics in 2023, FDA conducted more than 70 [GDUFA science and research projects](#) aligned with the 8 [FY 2023 GDUFA Research Priorities](#), which focused on using our resources to improve generic product development and regulatory assessment. The outcomes of this research prepared FDA to assess ANDAs referencing complex products, which ultimately increased patient access to complex generics that were practically impossible to develop a few years ago.

The [GDUFA Science and Research Program](#) translates to better access to medicines.

The GDUFA Science and Research Program supports the development of innovative and efficient approaches

Industry uses these approaches to develop generic drug products

Patients have better access to high-quality, safe, and effective generic products

The GDUFA science and research accomplishments in eight research areas detailed in the [GDUFA Science and Research Report](#) include:

- Impurities such as Nitrosamines
- Complex Active Ingredients
- Complex Dosage Forms and Formulations
- Complex Routes of Delivery
- Complex Drug-Device Combination Products
- Oral and Parenteral Generic Products
- Model-Integrated Evidence of Bioequivalence
- Artificial Intelligence and Machine Learning Tools

Additional Generic Drug Research

Other generic drug research focused on post-approval monitoring of generic products, generic product substitution, and attitudes among patients, caregivers, and prescribers related to the perceived therapeutic performance of generic products. Examples in 2023 included research with the reference listed drug (RLD) and generic products for lamotrigine extended-release tablets. The research results supported the appropriateness of FDA's recommendations for conducting a two-way crossover study to demonstrate the bioequivalence of lamotrigine extended-release tablets, and provided evidence to reinforce patient, caregiver, and prescriber confidence in approved generic lamotrigine extended-release tablets.

Additionally, research related to post-marketing surveillance of generic drugs assessed the substitutability of generic mixed amphetamine sulphate products for the treatment of attention-deficit/hyperactivity disorder. FDA also evaluated the nasal bioavailability of different formulations and delivery devices that may be used for a prospective generic naloxone nasal spray, indicated for the emergency treatment to reverse opioid overdose.

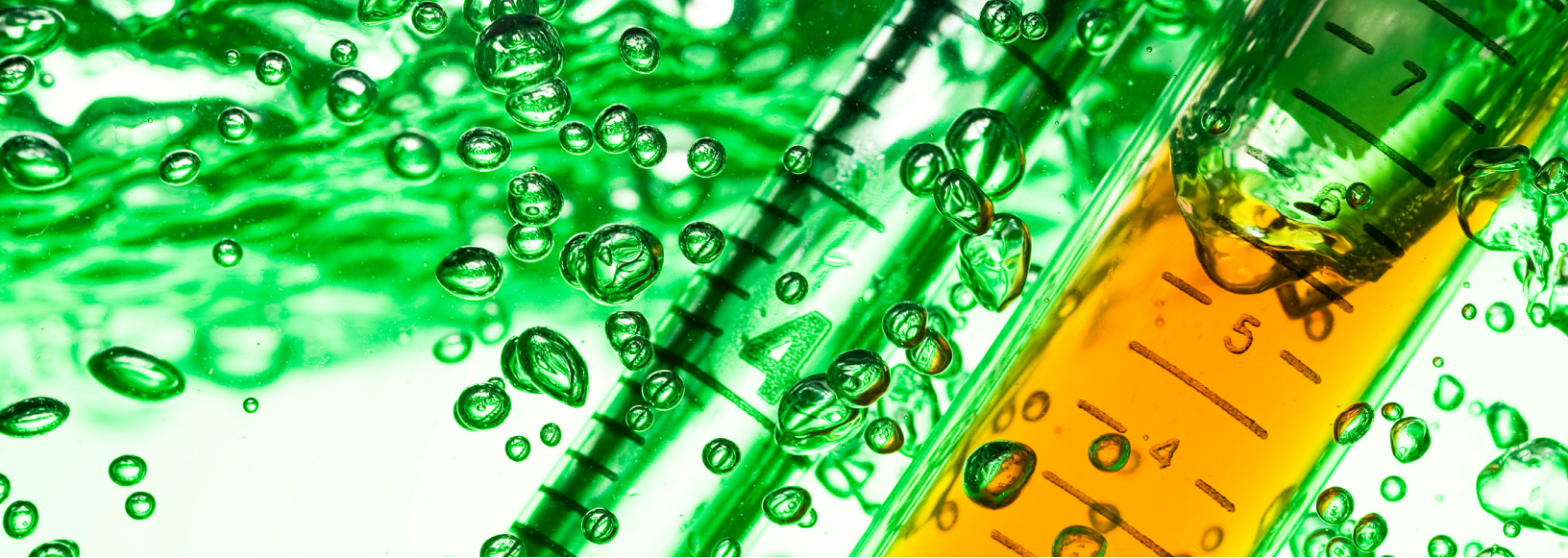
Communicating Research Results with Industry and Stakeholders

FDA hosted or co-hosted 12 public scientific meetings, webinars, trainings, and workshops in 2023 (see Appendix at the end of this Report). These events promote transparency, scientific research, and outreach, and enhance collaboration and communication through dialogue with academic experts and pharmaceutical industry representatives on numerous issues impacting generic drugs. Additionally, peer-reviewed scientific journals accepted 65 papers reporting our scientific findings.

CDER Impact Stories:

- [FDA shows generic lamotrigine extended-release tablets are bioequivalent to innovator drug in fully replicated crossover bioequivalence study](#)
- [Integration of Biorelevant Pediatric Dissolution Methodology into PBPK Modeling to Predict In Vivo Performance and Bioequivalence of Generic Drugs in Pediatric Populations: A Carbamazepine Case Study](#)

“Continual advances and emerging issues in pharmaceutical science create ongoing challenges for generic drug development. Efforts to advance science and research are the most effective way to address these challenges and facilitate the development of generic drugs for patients.”



Advancing Generic Drug Assessments through Bioequivalence

Bioequivalence (BE) is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same dose under similar conditions in an appropriately designed study.³ Accordingly, a brand-name drug product and a generic drug product are considered bioequivalent when there is not a significant difference in the rate and extent to which the active pharmaceutical ingredient becomes available at the site of the drug action when they are administered at the same dose under similar conditions in an appropriately designed study.^{4,5}

The BE of Abbreviated New Drug Applications (ANDAs):

OGD assesses the BE of ANDAs, including through the evaluation of studies that use pharmacokinetic, pharmacodynamic, and comparative clinical BE endpoints. OGD also assesses new methodologies to demonstrate BE, especially for generic drugs with complex dosage forms which pose unique challenges for demonstrating BE.

In 2023 FDA approved a generic drug noteworthy for its use of new methodologies, tacrolimus ointment, a second-line therapy for short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised patients. Rather than conducting the PSG-recommended in vitro permeation test (IVPT) study, the applicant proposed an alternative BE approach for the lower strength based on proportional release of the 0.03% and 0.1% strengths for the test and the reference listed drug products. Based on the totality of evidence provided to FDA, FDA found the alternative BE approach sufficient, and approved the 0.03% strength.

3 21 CFR 314.3 “Bioequivalence” definition found online at <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314/subpart-A/section-314.3#p-314.3>.

4 Id.

5 See preface of Approved Drug Products With Therapeutic Equivalence Evaluations, commonly known as the Orange Book, available at: <https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface>.

Modernizing the BE Assessment Process:

In 2023, OGD launched a new structured BE assessment tool – the Generic Drug Structured Assessment for Bioequivalence (GDSA-BE) – for two-way crossover in vivo pharmacokinetic (PK) BE studies for oral solid dosage form drug products. This tool officially signaled the change of bioequivalence assessment from narrative review to structured data with dynamic, interactive, and integrated collaboration capabilities. GDSA-BE is a BE assessment tool to enable a streamlined and efficient BE assessment and a powerful knowledge management tool, which aids consistent and well-informed regulatory decision making with direct access to multiple subject databases.

Training for External Stakeholders:

OGD provided trainings on BE recommendations for Scale-up and Post-approval Changes (SUPAC) and BE assessment for generic Narrow Therapeutic Index (NTI) drug products to the Pan American Health Organization (PAHO) member countries in the Americas. These trainings, provided through OGD's Global Generic Drug Affairs program, covered 1) FDA SUPAC guidance for oral immediate-release and modified-release products; 2) BE considerations for complex drug products with case studies; and 3) classification and BE assessment for NTI drugs. More than 250 participants from 26 countries attended the training. These trainings engaged discussion with key stakeholders, influencing the advancement and implementation of regulatory convergence initiatives in Latin America.



Policies to Strengthen Access to Safe, High-Quality, and Accessible Generic Drugs

As part of OGD’s efforts to improve patient access to generic drugs, we take steps to maximize scientific and regulatory clarity for generic drug developers regarding how they can meet the requirements for approval. Timely recommendations from FDA allow generic drug applicants to build that information into their research and development programs which can help them submit higher quality abbreviated new drug applications (ANDAs). As further described below, OGD makes its current thinking on regulatory and scientific issues known to applicants and the public.

Regulatory Guidances

We publish guidances that, when finalized, describe the Agency’s current thinking, and make recommendations to industry on regulatory and scientific issues related to generic drugs. FDA published 12 policy documents to support generic drug developers by clarifying FDA’s scientific and regulatory expectations and by bringing greater transparency to the generic drug assessment process, including with respect to the new GDUFA III enhancements. Guidances are available online in the [FDA Guidance Documents](#) database by choosing the “Generic Drugs” topic. Below are guidances issued in 2023.

Final Guidance:

- Cover Letter Attachments for Controlled Correspondence and ANDA Submissions (June 2023)

Draft Guidances:

- M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms (January 2023)
- Product-Specific Guidance Meetings Between the Food and Drug Administration and Abbreviated New Drug Applicants Under the Generic Drug User Fee Amendments (February 2023)
- Assessing Adhesion with Transdermal and Topical Delivery Systems for ANDAs (April 2023)

“Providing timely guidance allows generic drug applicants to build FDA recommendations into their research and development programs, which helps them submit higher-quality ANDAs.”

- Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs (April 2023)

MAPPs:

- Receiving and Processing a Request for Voluntary Withdrawal of an Approved ANDA (revised January 2023)
- Assessment of Bioequivalence Studies with Clinical Endpoints in ANDAs (revised May 2023)
- ANDA Suitability Petitions (revised September 2023)
- Filing Review of Abbreviated New Drug Applications (revised October 2023)
- Good Abbreviated New Drug Application Assessment Practices (revised October 2023)
- Generic Drug Labeling Revisions Under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (revised December 2023)

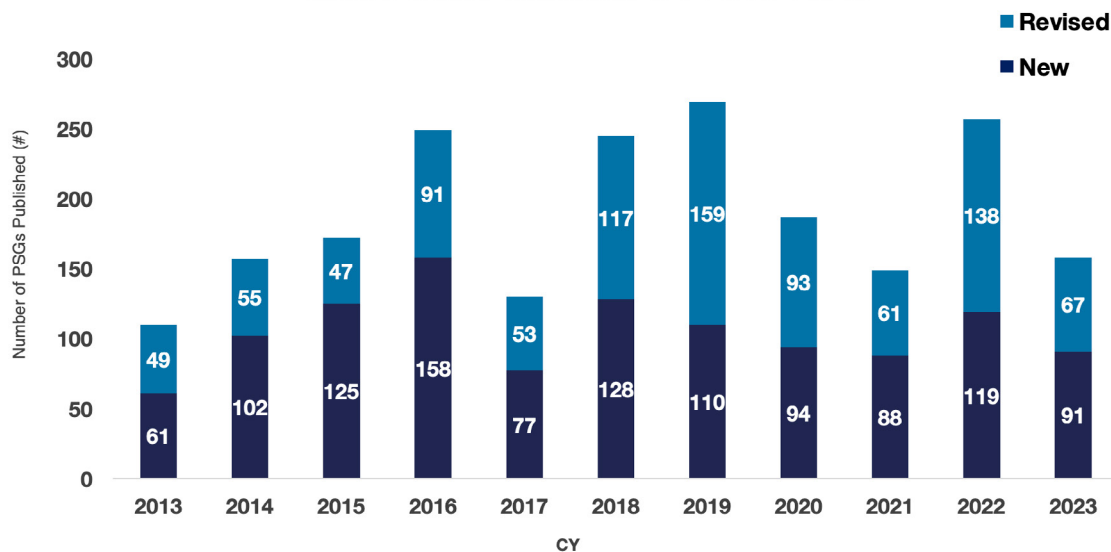
Federal Register Notices (FRNs) and Other Policy Resources:

- Fiscal Year 2023 Generic Drug Science and Research Initiatives Workshop; Public Workshop; Request for Comments (February 2023)
- List of Off-Patent, Off-Exclusivity Drug Products without an Approved Generic (Website updated June 2023 and December 2023)
- [The Generic Drug Savings Report](#)

Product-Specific Guidances (PSGs)

FDA regularly publishes product-specific guidances (PSGs), which describe the Agency’s current thinking and expectations on how to develop generic drug products that are therapeutically equivalent to specific reference listed drugs. PSGs further facilitate generic drug product availability and assist generic drug developers with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval. OGD develops PSGs based on public health priorities, requests from industry, and current and anticipated patient and industry needs, consistent with OGD’s [GDUFA III](#) commitments. In 2023 we issued a total of 158 new and revised PSGs (91 of which were for complex products) including 121 for products (69 for complex products) with no approved ANDA at the time of the PSG publication. Additionally, 33 PSGs were published to add an efficient in vitro BE option.

Total PSGs Published CY 2013-2023



Drug Competition Action Plan (DCAP)

Beyond directly approving generic drug applications, OGD continued its execution of FDA's Drug Competition Action Plan (DCAP). Draft and final guidances and MAPPs help to ensure that current and prospective ANDA applicants have the information they need to successfully submit high-quality ANDAs and to take advantage of the newly implemented GDUFA III commitments, including increased opportunities for meetings and other interactions with applicants. Notable deliverables in 2023 included revised draft guidances related to the design and conduct of studies for evaluating transdermal and topical delivery systems submitted in support of ANDAs.

Spotlight On Generic Drug Policy

In February 2023, OGD published a new draft guidance for industry, ["Product-Specific Guidance Meetings Between FDA and ANDA Applicants Under GDUFA."](#) This guidance provides recommendations on PSG meetings between FDA and prospective applicants or applicants that have submitted an ANDA; information on requesting and conducting PSG teleconferences, pre-submission PSG meetings, and post-submission PSG meetings, which are outlined in the GDUFA III Commitment Letter; and procedures for well-managed PSG meetings that can ensure meetings are scheduled and conducted in accordance with the timeframes set forth in the GDUFA III Commitment Letter.

Competitive Generic Therapies (CGT)

As part of the continued implementation of the congressionally established CGT pathway, we have approved more than 370 generic drug products with a CGT designation, including 119 in 2023. In 2023, of the approved CGT-designated drugs eligible for CGT exclusivity, approximately 41 drug products began commercial marketing within an average of 23 days from their approval.



Monitoring and Ensuring Generic Drug Safety

The FDA follows a [rigorous assessment process](#) to ensure that, compared to the brand-name drug, a generic drug has the same:

- Active ingredients (the ingredients that treat a condition or symptoms)
- Strength
- Dosage form (for example: tablet, capsule, cream, patch, or liquid)
- Route of administration (for example: oral, topical, inhalation, or injection)
- Conditions of use
- Labeling (with certain exceptions)

Part of this assessment process includes evaluating and considering factors to ensure generic drugs are safe and therapeutically equivalent to their reference listed drugs (RLDs). This includes review of excipient differences and impurities. OGD reviews pre-approval serious adverse event (AE) reports from Bio-Investigational New Drugs (IND) and non-IND bioequivalence studies intended to support abbreviated new drug applications (ANDAs). OGD also supports the implementation of Risk Evaluation and Mitigation Strategies (REMS) programs for generic drugs that are subject to a REMS.

As part of ensuring that generic drugs are therapeutically equivalent to the RLD, OGD also evaluates the user interface of generic drug-device combination products to assess whether there are design differences which may impact safe and effective substitution for the RLD. This has, at times, posed challenges for the generic drug industry so OGD supported industry around the development of generic drug-device combination products through the workshop *“Identifying, Developing, and Evaluating Drug-Device Combination Products.”*

“OGD excels in clinical and pharmacologic/toxicologic scientific analyses of comparative clinical, safety, and surveillance data to ensure that generic drug products are therapeutic equivalents to their RLDs and safe for use by the American public.”

Safety Surveillance for Generic Drugs

OGD leads many safety and surveillance activities to ensure generic drugs continue to be therapeutically equivalent to their RLDs. OGD monitors and evaluates generic drugs after approval by investigating and analyzing generic drug quality, adverse event reports and trends, follow generic drug distribution patterns, and identify emerging safety issues that might indicate a product is not therapeutically equivalent. OGD also assesses drug quality issues for potential generic medication products recalls.

One example of OGD's activities to support access to safe, effective, and therapeutically equivalent generic drugs is the action taken on the Newly Identified Safety Signal (NISS) for Accord Healthcare's generic tacrolimus oral capsules and information demonstrating that the product is not bioequivalent to its RLD. As a result of its review of this new information, FDA changed the therapeutic equivalence rating for Accord Healthcare's tacrolimus oral capsules from AB to BX.⁶

Supporting the Assessment of Novel Impurities

OGD continued to lead in assessing and educating industry on nitrosamine impurities in 2023. Such efforts included collaboration with the FDA's National Center for Toxicologic Research to identify testing conditions for nitrosamines and support for the publication of the guidance "Recommended Acceptable Intake Limits for Nitrosamine Drug Substance-Related Impurities (NDSRIs)," as well as support for the FDA website that provides recommended limits for a variety of potential NDSRIs and the educational workshop "Mitigation Strategies for Nitrosamine Drug Substance Related Impurities." The workshop brought regulators, academia, and industry together to discuss ongoing research and current challenges in the assessment of nitrosamine-related risks.

6 For more information on this action, see FDA is Changing the Therapeutic Equivalence Rating for Accord Healthcare Inc.'s Generics of Prograf (tacrolimus) Oral Capsules, <https://www.fda.gov/drugs/drug-safety-and-availability/fda-changing-therapeutic-equivalence-rating-accord-healthcare-incs-generics-prograf-tacrolimus-oral> (Sept. 18, 2023).

The FDA Generic Drug Program – A Special Thank You to Our Collaborators

OGD benefits from and relies on the efforts of many FDA offices that cooperate within the program, including:

- Center for Biologics Evaluation and Research
- Center for Devices and Radiological Health
- Center for Drug Evaluation and Research
 - Office of Communications
 - Office of Compliance
 - Office of Management
 - Office of Medical Policy
 - Office of New Drugs
 - Office of Pharmaceutical Quality
 - Office of Regulatory Policy
 - Office of Strategic Programs
 - Office of Surveillance and Epidemiology
 - Office of Translational Sciences
- National Center for Toxicological Research
- Office of the Chief Counsel
- Office of the Commissioner
- Office of Executive Programs
- Office of Regulatory Affairs

We would like to thank our internal collaborators, especially the Office of Pharmaceutical Quality, who greatly contributed to our successes in 2023. We look forward to our future collaborations that will help further increase access to generic drugs for the American public.

Appendix

2023 Conferences, Public Meetings, Webinars, Trainings, and Workshops

[Small Business and Industry \(SBIA\) Webinar: A Deep Dive: FDA Draft Guidance on Statistical Approaches to Establishing Bioequivalence](#)

This webinar provided a deeper look into FDA's draft guidance for industry titled [Statistical Approaches to Establishing Bioequivalence](#) with recommendations to sponsors and applicants who intend to use equivalence criteria when analyzing in vivo or in vitro bioequivalence studies for investigational new drugs, new drug applications, abbreviated new drug applications, and supplements to these applications.

[Generic Drugs Forum \(GDF\) 2023: Celebrating 10 Years of the GDF](#)

Subject matter experts from FDA explained the ANDA assessment process in detail, presented case studies, and provided practical advice to current and prospective generic drug applicants.

[FDA and Center for Research on Complex Generics Co-Hosted Workshop: Considerations for and Alternatives to Comparative Clinical Endpoint and Pharmacodynamic Bioequivalence Studies for Generic Orally Inhaled Drug Products](#)

Scientific and regulatory perspectives for using in vitro, in vivo, and in silico studies as alternatives to comparative clinical endpoint bioequivalence studies and pharmacodynamic bioequivalence studies associated with establishing the equivalence of local drug delivery for suspension-based metered dose inhalers and dry powder inhalers.

[SBIA Webinar: Navigating the First ICH Generic Drug Draft Guideline "M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms"](#)

This webinar provided a deeper look into the FDA draft guidance for industry which followed the International Council for Harmonisation (ICH), Technical Requirements for Pharmaceuticals for Human Use.

[FDA and Center for Research on Complex Generics Co-Hosted Training: Drug-Device Combination Products 101: Identifying, Developing, and Evaluating Drug-Device Combination Products](#)

This training discussed FDA's regulatory expectations and practices for pre-ANDA assessment and ANDA review of generic drug-device combination products, especially those with complex device constituent parts.

[FY 2023 Generic Drug Science and Research Initiatives Public Workshop](#)

This public workshop provided an overview of the status of science and research initiatives for generic drugs and an opportunity for public input on these initiatives.

[SBIA Webinar: A Deep Dive: GDUFA III Scientific Meetings](#)

This webinar provided a deeper look into new enhancements or changes under GDUFA III to the generic drug program's pre-ANDA and ANDA process as it relates to scientific meetings that help prospective applicants looking to develop new generic drug products.

[2023 Financial Transparency and Efficiency of the Prescription Drug User Fee Act, Biosimilar User Fee Act, and Generic Drug User Fee Amendments](#)

This was an annual public meeting and opportunity for public comment on "Financial Transparency and Efficiency of the Prescription Drug User Fee Act, Biosimilar User Fee Act, and Generic Drug User Fee Amendments."

[FDA and Center for Research on Complex Generics Co-Hosted Workshop: Mitigation Strategies for Nitrosamine Drug Substance Related Impurities: Quality and Bioequivalence Considerations for Generic Products](#)

This workshop discussed the risks of forming N-nitrosamine drug substance related impurities (NDSRIs) in certain drug products, strategies to mitigate these risks, and considerations in assessing the safety risks of NDSRIs.

[SBIA Workshop: Advancing Generic Drug Development: Translating Science to Approval 2023](#)

This workshop communicated how outcomes from FDA's GDUFA Science and Research Program guide and facilitate generic drug development, regulatory assessment, and approval.

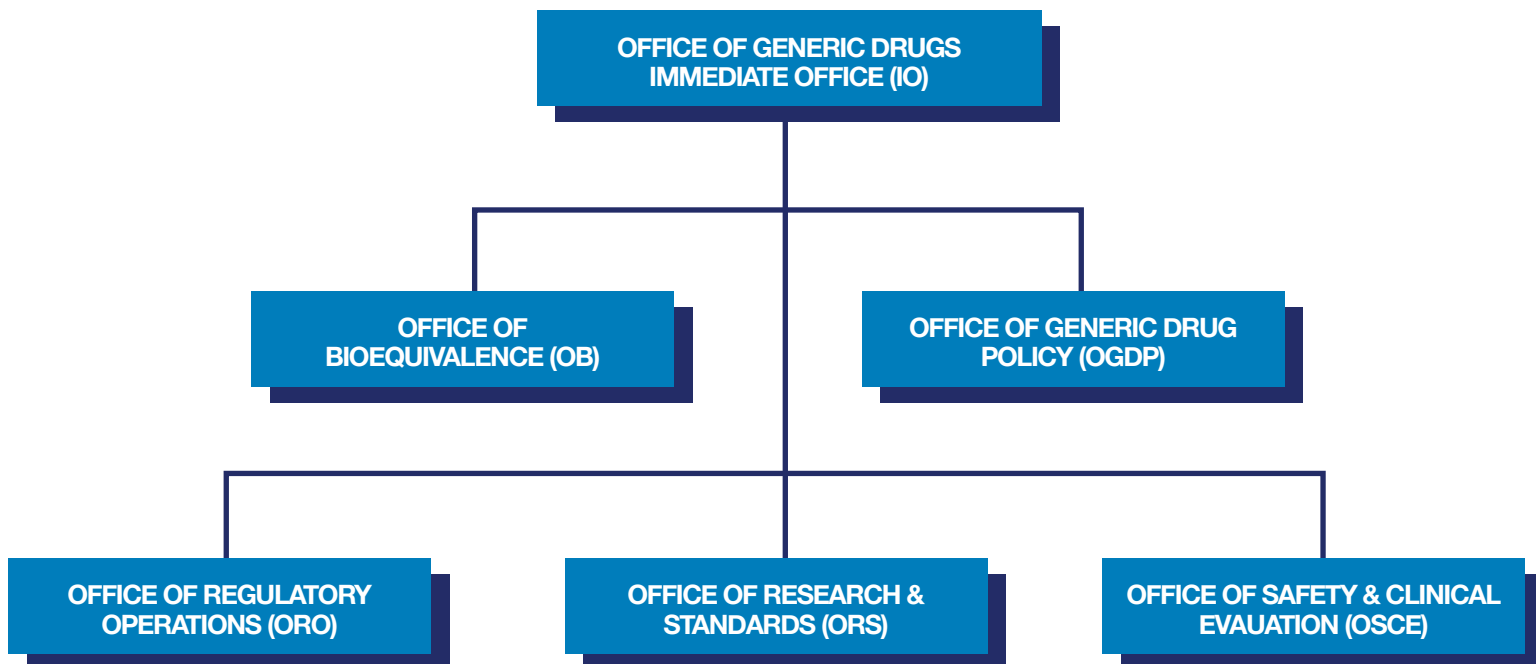
[FDA and Center for Research on Complex Generics Co-Hosted Workshop: Advances in PBPK Modeling and its Regulatory Utility for Oral Drug Product Development](#)

This workshop discussed the challenges, experiences, and advances for the development of physiologically based pharmacokinetic (PBPK) oral absorption modeling to support the establishment of bio-predictive in vitro testing (e.g., dissolution). It also addressed risks associated with the extrapolation of BE in various contexts, such as from a fasting to a fed state, assessing BE in pediatrics, and with other risk-based BE assessments for oral products.

[FDA and Center for Research on Complex Generics Co-Hosted Workshop: Characterization of Complex Excipients](#)

This workshop discussed the scientific principles and practical considerations that inform current FDA thinking about the characterization of complex excipients and formulations, to support generic product development and assessment. The workshop provided an update on the progress of research activities funded by the GDUFA science and research program, explored challenging issues for generic product development and assessment, identified areas that need further research, and discussed opportunities for coordination and collaboration among the FDA, generic drug industry, academic institutions, excipient vendors, contract research organizations, consultants, and other stakeholders.

Office of Generic Drugs Organization Chart



Links to Select Online Resources

- [About the Office of Generic Drugs](#)
- [Activities Report of the Generic Drug Program](#)
- [Approvals & Reports](#)
- [CDER Small Business and Industry Assistance \(SBIA\)](#)
- [Competitive Generic Therapy \(CGT\) Approvals](#)
- [FDA Drug Competition Action Plan](#)
- [First Generic Drug Approvals](#)
- [First Generic Drug Approvals Previous Years](#)
- [Generic Drug Program](#)
- [Generic Drug User Fee Amendments \(GDUFA\)](#)
- [GDUFA III Commitment Letter](#)
- [GDUFA Science and Research](#)
- [Global Generic Drug Affairs](#)
- [Off-Patent, Off Exclusivity List](#)
- [Orange Book](#)
- [Paragraph IV \(PIV\) Patent Certifications](#)
- [Product-Specific Guidances](#)
- [Upcoming Complex and Non-Complex PSGs](#)

Helpful Acronyms and Abbreviations

Acronym/Abbreviation	What It Means
ANDA	Abbreviated New Drug Application
AE	Adverse Events
BA	Bioavailability
BE	Bioequivalence
CDER	Center for Drug Evaluation and Research
CGT	Competitive Generic Therapy
CRL	Complete Response Letter
DCAP	Drug Competition Action Plan
DRL	Discipline Review Letter
FDA	Food and Drug Administration
FRN	Federal Register Notice
GDUFA	Generic Drug User Fee Amendments
IR	Information Request
IVPT	In Vitro Permeation Test
MAPP	Manual of Policies and Procedures
NDA	New Drug Application
OGD	Office of Generic Drugs
OND	Office of New Drugs
OPQ	Office of Pharmaceutical Quality
ORP	Office of Regulatory Policy
OSE	Office of Surveillance and Epidemiology
OTS	Office of Translational Sciences
Orange Book	Approved Drug Products with Therapeutic Equivalence Evaluations
PBPK	Physiologically Based Pharmacokinetic
PK	Pharmacokinetic
PSG	Product-Specific Guidance
REMS	Risk Evaluation and Mitigation Strategy
RLD	Reference Listed Drug
SBIA	Small Business & Industry Assistance Program



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We Welcome Your Feedback

OGD welcomes feedback from stakeholders and the public. We will continue to communicate with industry as we work to meet GDUFA III and DCAP goals.

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