State of Generics 2025

Iilun Murphy, M.D.
Director, Office of Generic Drugs
CDER

FDA U.S. FOOD & DRUG ADMINISTRATION


We care about enhancing access to generic drugs
WE ARE THE GENERIC DRUG PROGRAM

FY 2025 Generic Approvals

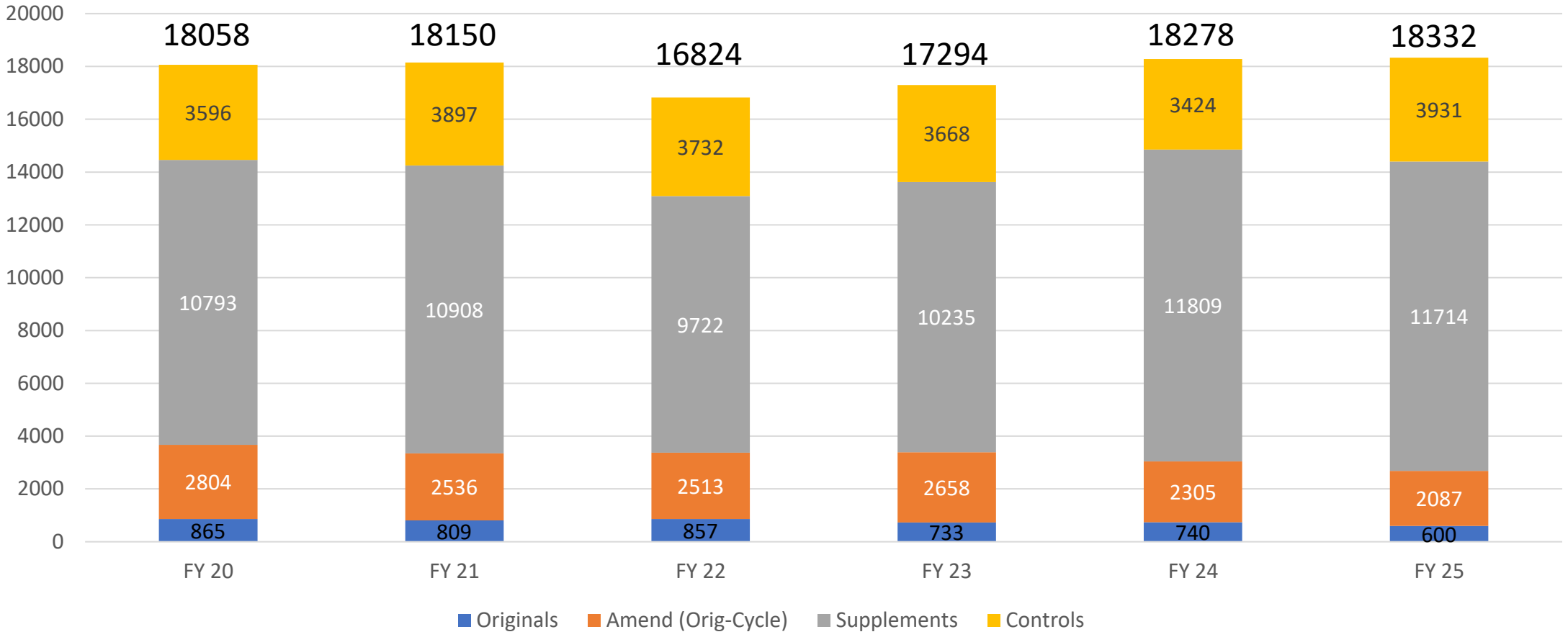
939 ANDAs approved or tentatively approved, including:

- 92 First Generic Drug Approvals
- 107 generics with Competitive Generic Therapy (CGT) designation
- 125 complex generics

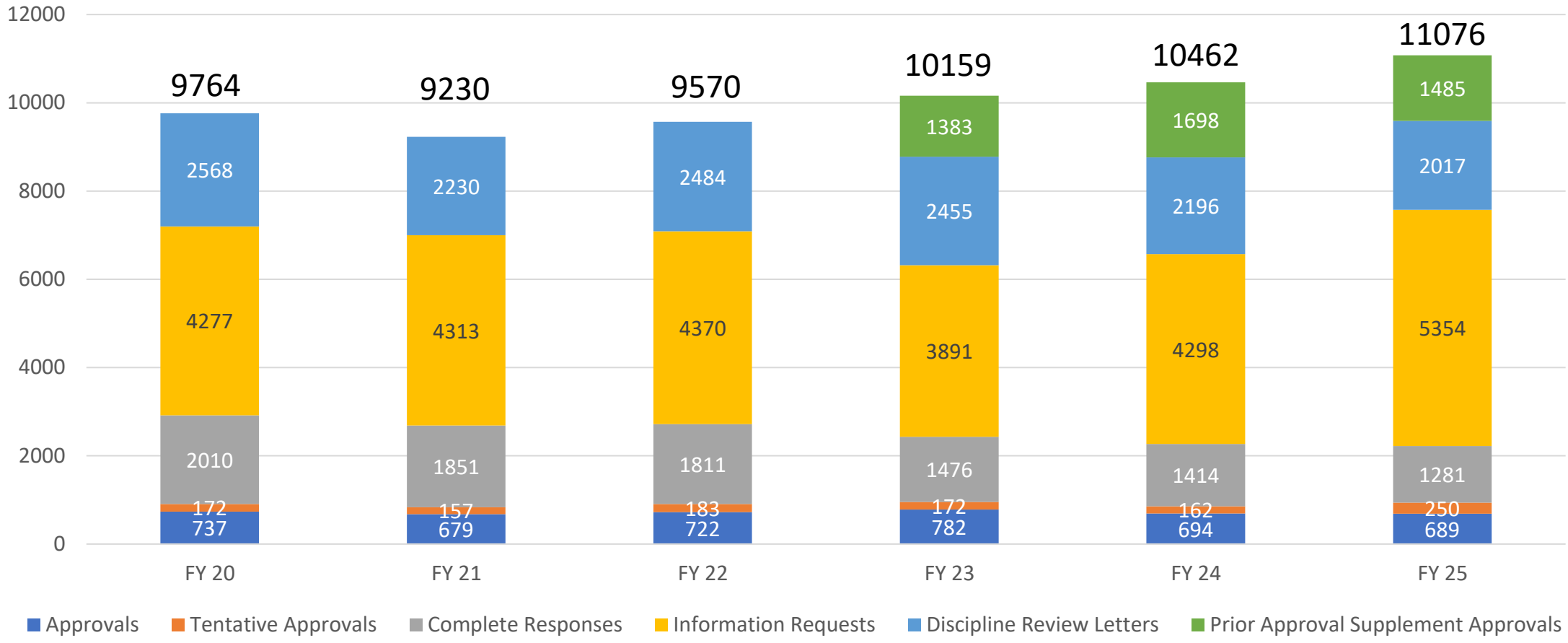
Highlighted 2025 First Generics

Generic Name	Brand Name	Indication	Approval Date
Liraglutide Injection	Saxenda	Chronic weight management	August 2025
Iron Sucrose Injection	Venofer	Iron deficiency anemia in CKD/dialysis	July 2025
Sitagliptin + Metformin XR	Janumet XR	Type 2 diabetes	June 2025
Rivaroxaban	Xarelto	Anticoagulation	May 2025
Siponimod	Mayzent	Multiple sclerosis	April 2025

ANDA Program: Key Receipts



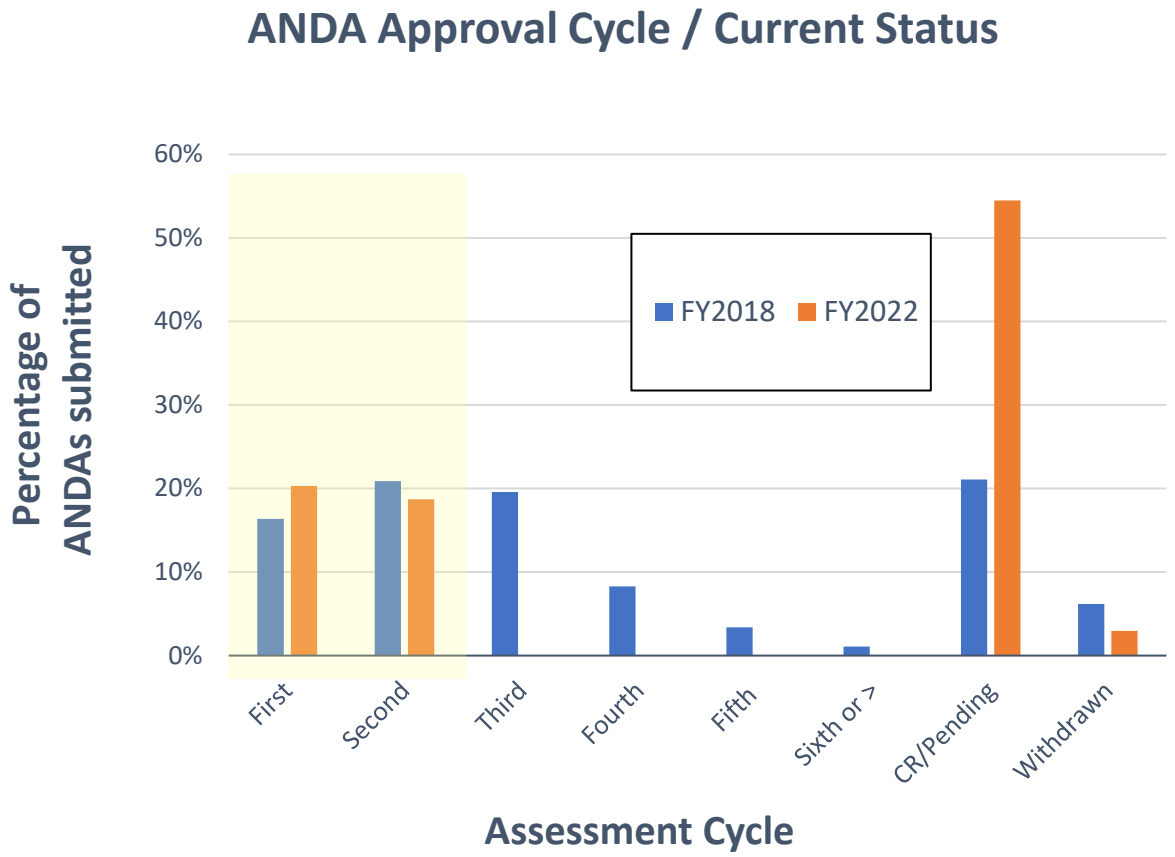
ANDA Program: Key Actions



FY2018 & FY2022 ANDA Submissions

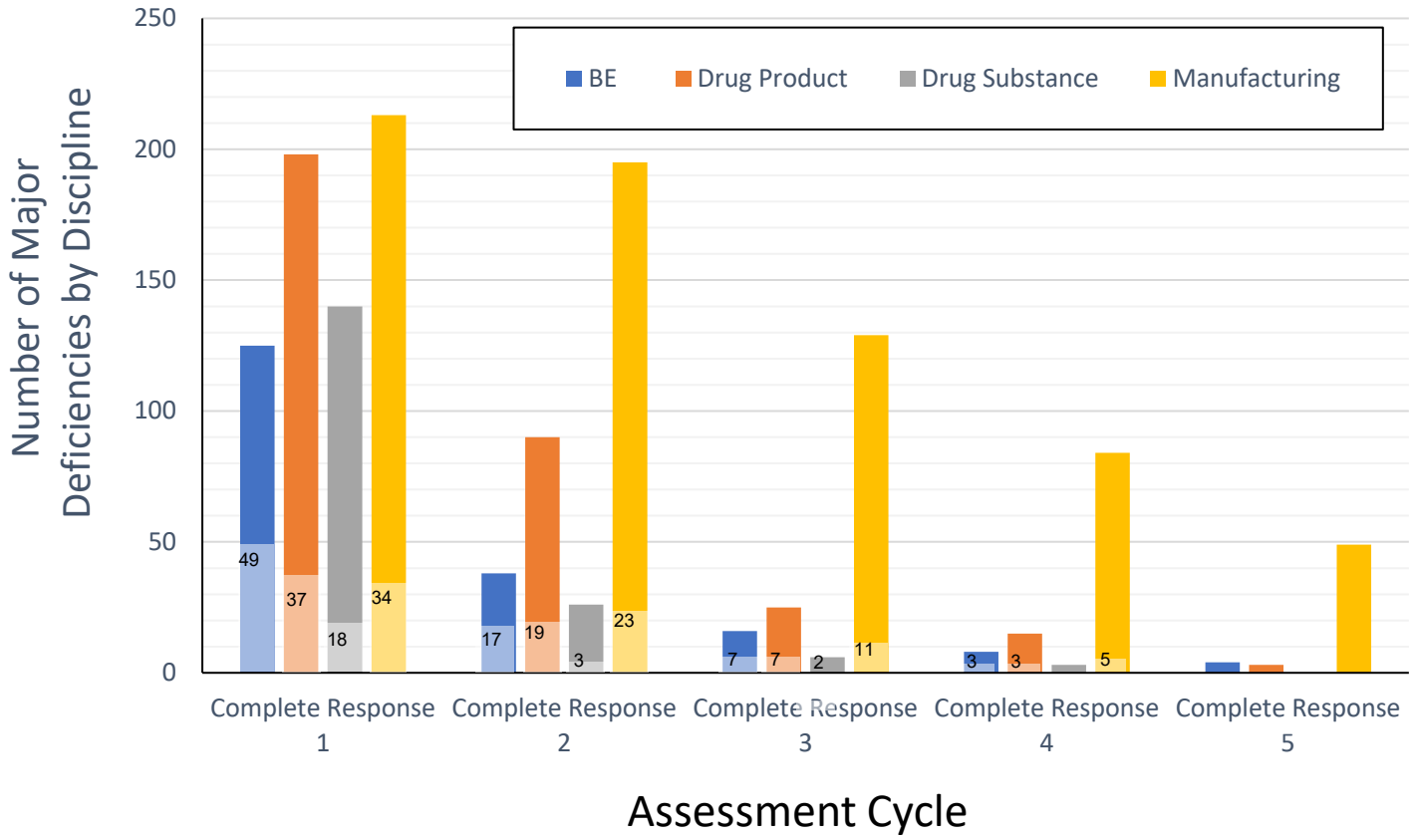
Approximately 40% of FY18 and FY22 ANDAs were approved by the second assessment cycle

- Complex products accounted for ~14% and ~17% of ANDA submissions in FY18 and FY22, respectively. Approximately 25% of these complex product ANDAs were approved by the second cycle.
- ANDAs submitted in FY18 and FY22 provide sufficient time for at least two assessment cycles. Most FY18 ANDAs should be close to final action status whereas most FY22 ANDAs in CR will come back for third cycle.



Major Deficiencies by Discipline

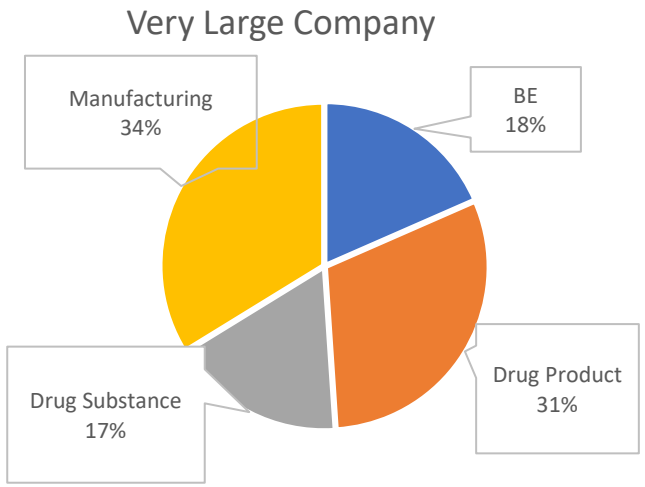
- ANDAs submitted in FY18 were more likely to have a major manufacturing deficiency at each review cycle. Other major deficiencies were generally resolved by second or third assessment cycle.

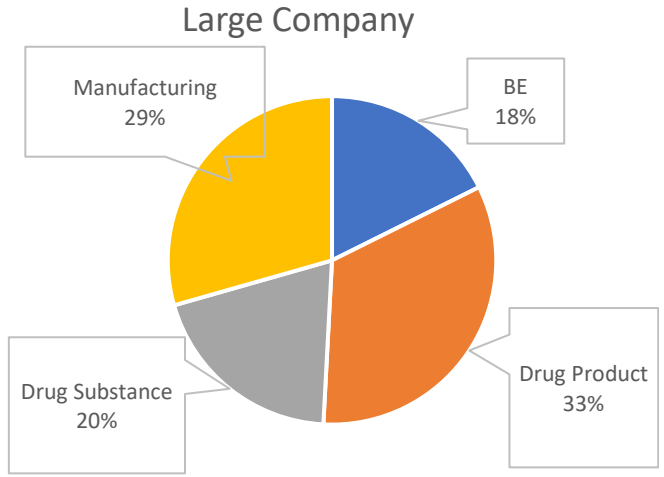


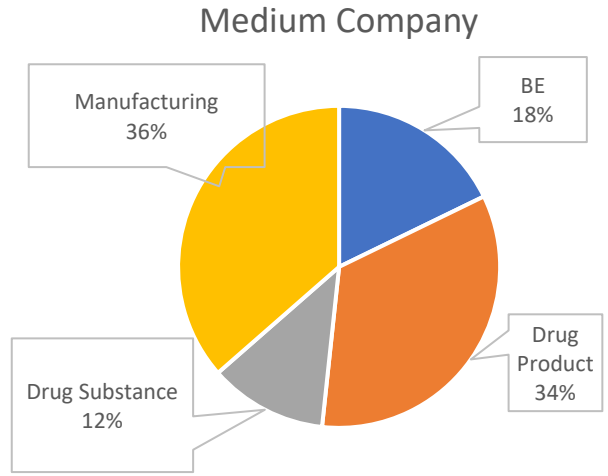
- Complex products (lighter shaded data with labels) generally make up a larger percentage of major BE (~40%) and Drug Product (~20%) deficiencies in the first CR even though they are ~14% of ANDA submissions in FY18.
- Manufacturing deficiencies do not appear to be dependent on product complexity
  - Manufacturing major for complex products is ~14%, which is similar percentage of complex ANDA submissions (~14%) in FY18.

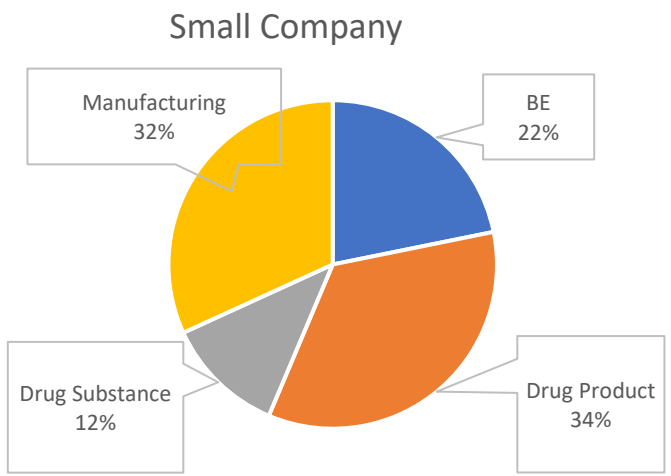
First Cycle Major Deficiencies

- Approximately 300 different companies submitted ANDAs in FY18 & FY22.
  - **Very Large Company**[1] (>100 ANDAs), **Large** (≤ 100 ANDAs ≥ 20), **Medium** (≤ 19 ANDAs ≥6), **Small** (< 6 ANDAs)
- Very large companies submitted half of ANDAs.
  - Complex product ANDAs make up 18% of ANDAs submitted by Very Large and Small companies. 10% of ANDAs submitted by Large and Medium sized companies are for complex products.
- Manufacturing and Drug Product are most common major deficiencies at the first cycle CR regardless of company size.





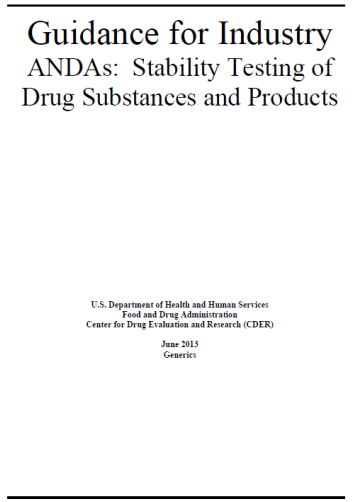




1. Company size is based on approved ANDAs held by the parent company in 2023. GDUFA Program Fee does not include a very large company category. Here very large was defined as having more than 100 ANDAs.

Refuse-To-Receive Top Issues

1. **Incomplete stability data**
2. Formulation sameness
3. 356h form incomplete

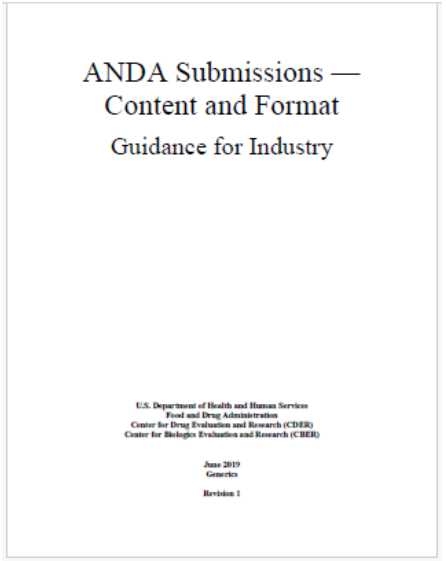


Guidance for Industry

ANDAs: Stability Testing of Drug Substances and Products

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2013
Generics



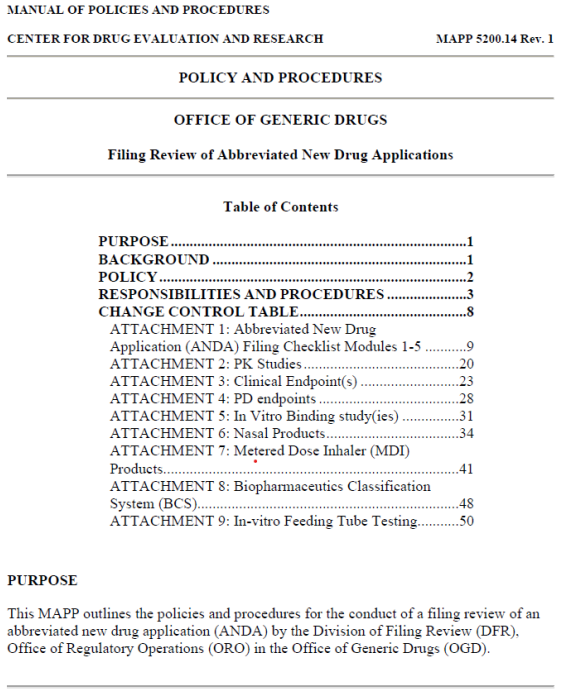
ANDA Submissions — Content and Format

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2019
Generics

Revision 1



MANUAL OF POLICIES AND PROCEDURES

CENTER FOR DRUG EVALUATION AND RESEARCH — MAPP 5200.14 Rev. 1

POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

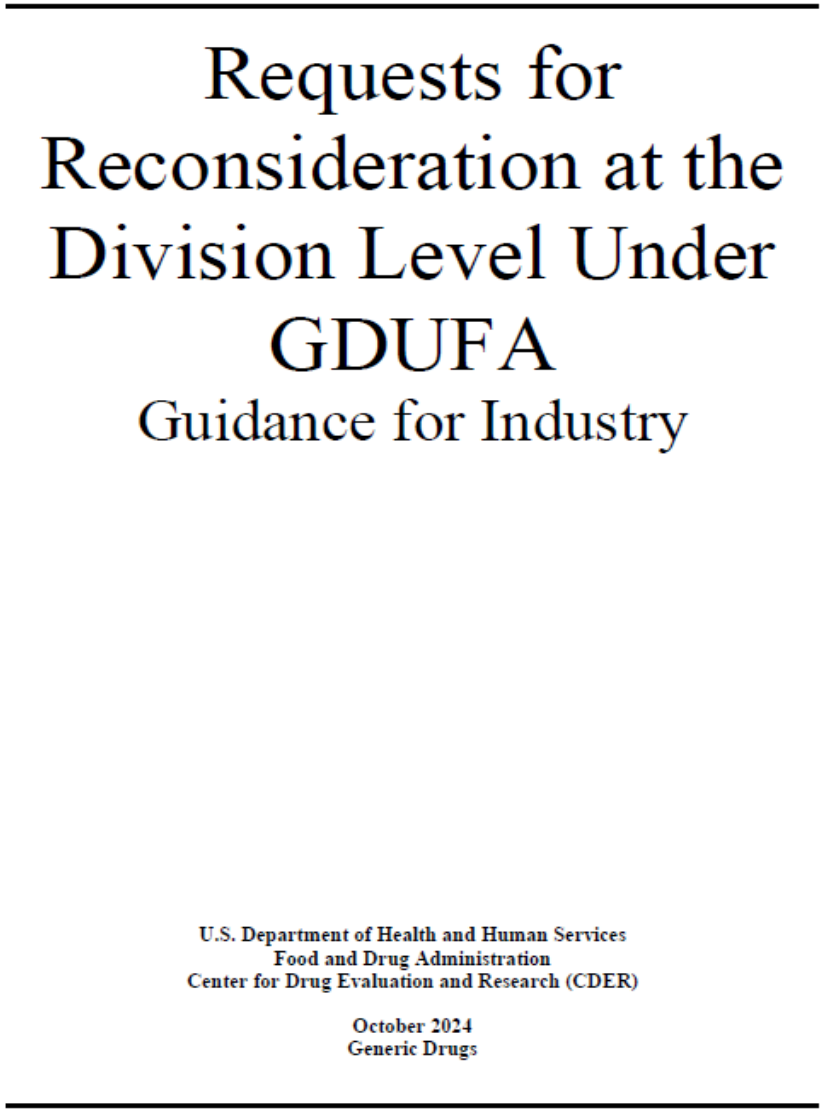
Filing Review of Abbreviated New Drug Applications

Table of Contents

PURPOSE

This MAPP outlines the policies and procedures for the conduct of a filing review of an abbreviated new drug application (ANDA) by the Division of Filing Review (DFR), Office of Regulatory Operations (ORO) in the Office of Generic Drugs (OGD).

Requests for Reconsideration and Reclassifications



Requests for Reconsideration at the Division Level Under GDUFA

Guidance for Industry

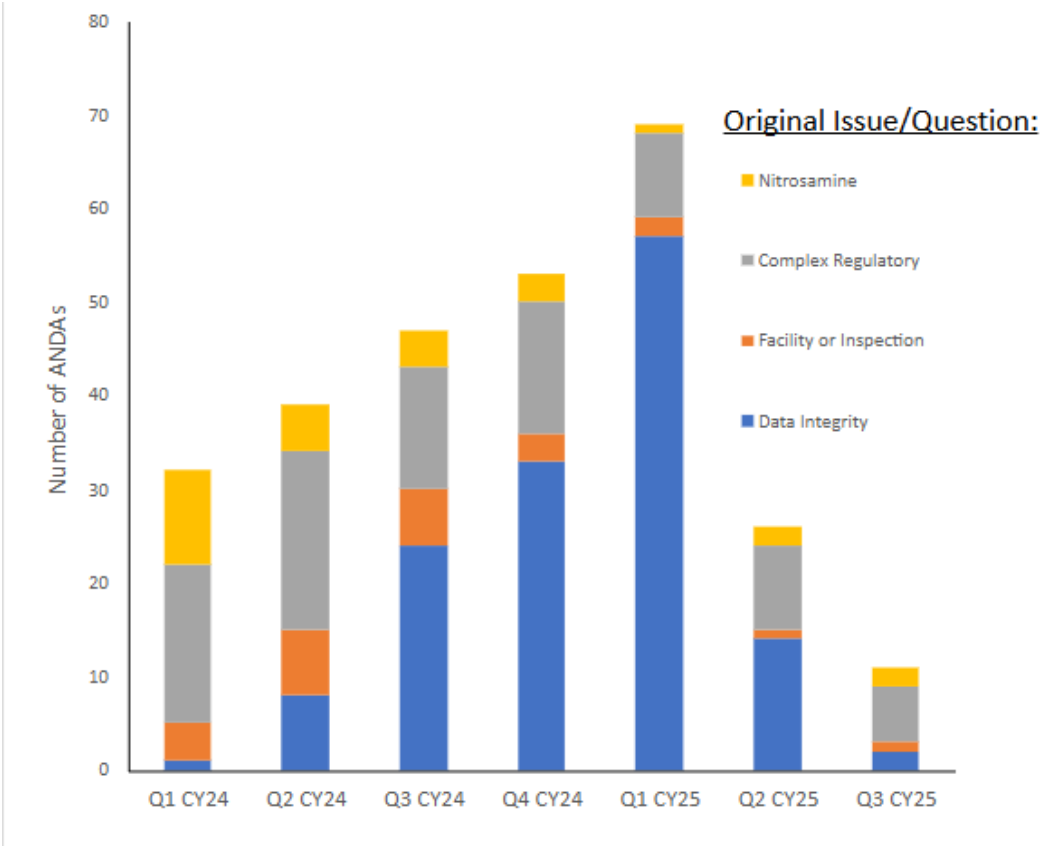
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

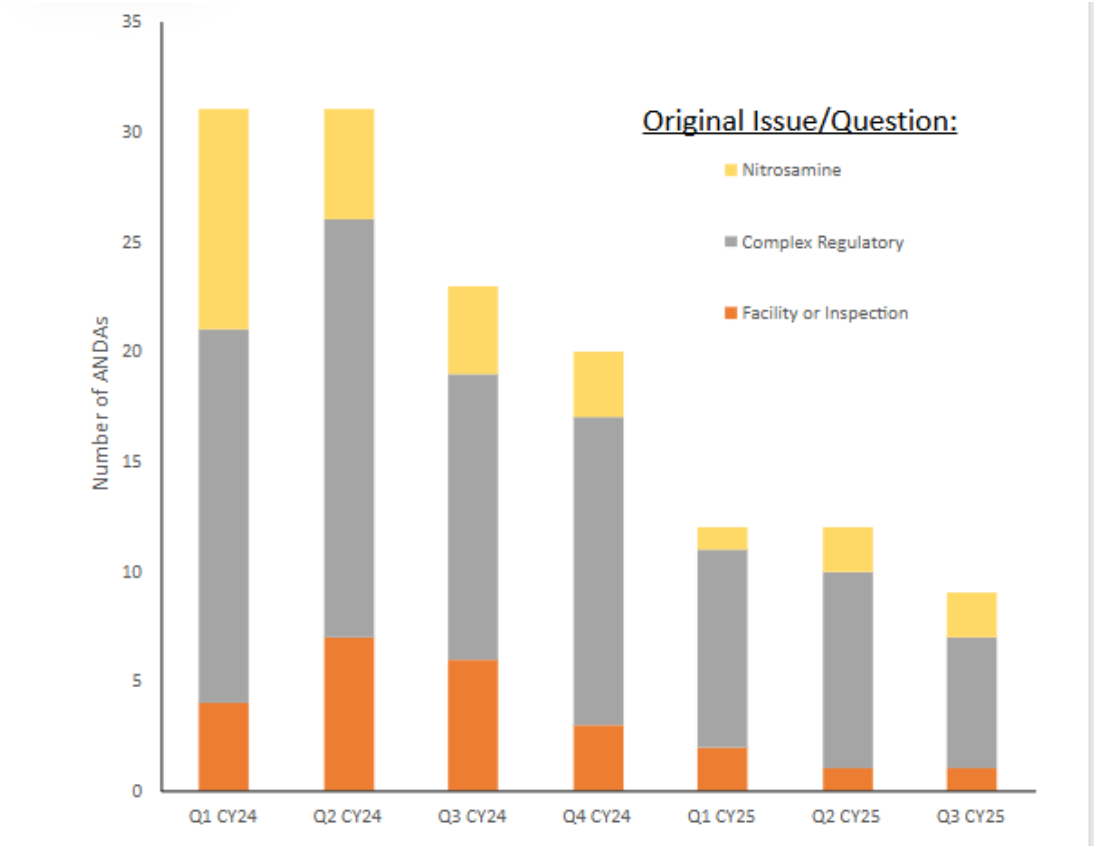
October 2024
Generic Drugs

Identifying and Resolving Issues Before they Become Deficiencies

- GDUFA III initiatives and opportunities for enhanced communication throughout the generic drug process to help identify resolutions to (potential) major deficiencies.
  - Controlled correspondences, development meetings, discipline review letters (DRL), information requests (IR), Mid-cycle review meetings, post-CR meetings, etc.
- Targeted workshops on development issues for specific classes of products and issues.
  - SBIA workshops and webinars are informational sessions on processes, best practices, and common issues/deficiencies with generic drug development (pre-ANDA) and ANDAs. These are recorded and publicly available: https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/cder-small-business-and-industry-assistance-sbia-learn
  - Center for Research on Complex Generics (CRCG) includes interactive workshops on complex scientific issues and considerations. These are recorded and publicly available: https://www.complexgenerics.org/education-training/
- FDA strives to provide clarity, where possible, through general guidance and product-specific guidance (PSG) as well as to make regulatory and scientific research findings publicly accessible through presentations, publications, and white papers.

Past Goal Date ANDAs





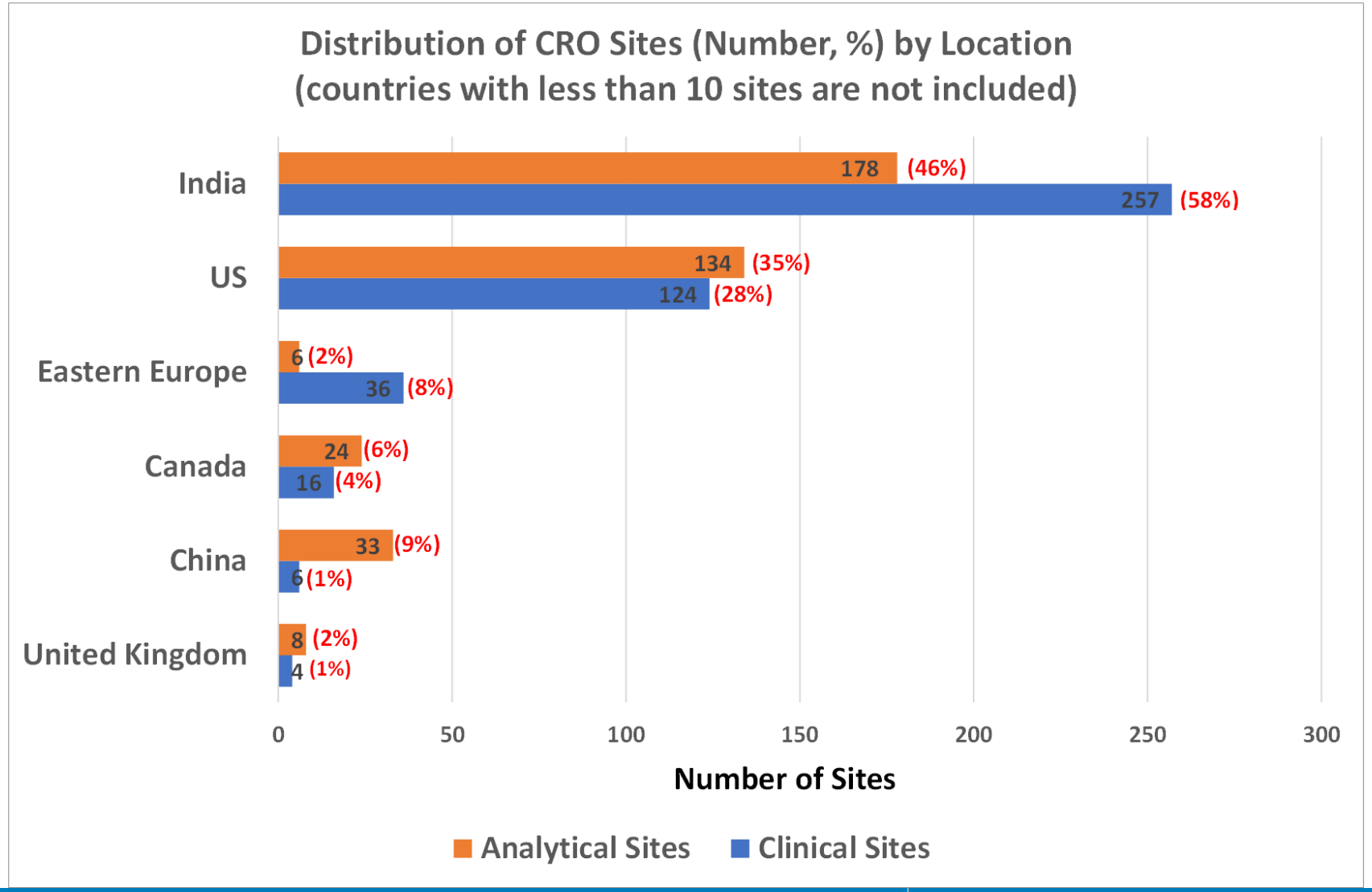
Data Integrity Reminders

FDA requires high-quality data that is accurate, consistent, and reliable.

FDA and OGD require industry to maintain the integrity of data throughout the data lifecycle.

Companies with data integrity issues in their submissions often have to go back and redo studies, resulting in lost productivity.

Distribution of Global Clinical and Analytical CRO sites



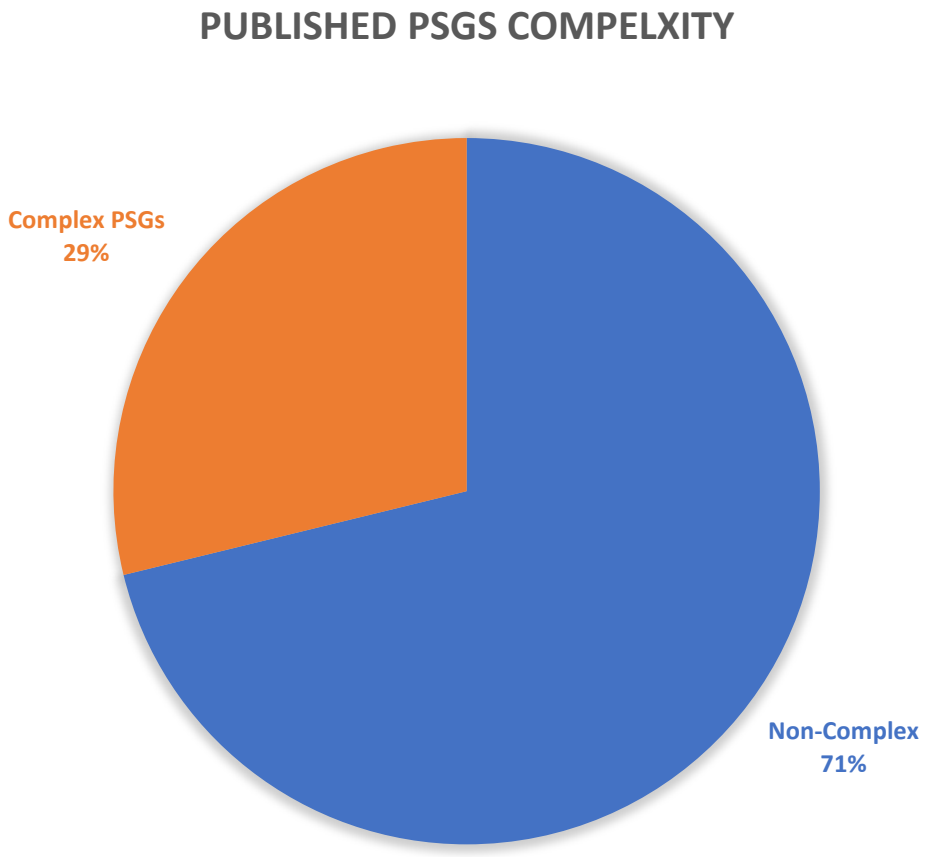
Supporting Complicated Generic ANDAs

FY 2025 Guidances

- 3 Final Guidances
  - Requests for Reconsideration at the Division Level Under GDUFA (10/17/24)
  - M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms (10/31/24)
  - ANDAs: Pre-Submission Facility Correspondence Related to Prioritized Generic Drug Submissions (6/16/2025)
- 1 Draft Guidance
  - M13B: Bioequivalence for Immediate-Release Solid Oral Dosage Forms: Additional Strengths Biowaiver (6/2/25)

FY 2025 Regulatory Enhancements

900+ product-specific guidances (PSGs), which provide recommendations on developing individual generic drug products



Highlighted May 2025 Draft Guidance: M13B Bioequivalence for Immediate-Release Solid Oral Dosage Forms: Additional Strengths Biowaiver

- Second ICH-endorsed “harmonized” guidance for generic drugs
- Represents the harmonization efforts of 22 global organizations
- Describes waivers of bioequivalence (BE) studies for one or more additional strengths of a drug product in an application where in vivo BE has been demonstrated for at least one of the strengths

The adoption and implementation of M13B will:

- Result in harmonization of current regional guidelines/guidances
- Reduce the need for additional in vivo BE studies
- Support streamlined global drug development

Science Drives Policy
Generics

GDUFA Science and Research Program

Fosters early engagement between FDA and the generic drug industry

- provides opportunities for better informed engagement post-submission in scientific meetings
- facilitates engagement with prospective applicants through pre-ANDA meetings
- collaborates with generic industry to determine the GDUFA Regulatory Science and Research Priority Initiatives

Aims to improve efficiency with which generic drugs can be developed and assessed

- bridges knowledge gaps in development of generic drugs
- establishes and clarifies the scientific framework for ANDA development, submission, and assessments
- enables efficient approaches for developing generic products
- helps FDA assess the BE and quality of complex generic products

Enhances generic drug development and approval

- expands understanding of drug products, including complex products
- contributes to the development of advanced methods to characterize product quality and performance
- makes it more feasible for manufacturers to develop generic drugs

FY 2025 Generic Drug Science and Research Priorities

- Develop methods for generics to address impurities, such as nitrosamines
- Enhance the efficiency of bioequivalence approaches for
  - complex active ingredients
  - complex dosage forms and formulations
  - complex routes of delivery
  - complex drug-device combination products
  - oral and parenteral generic products
- Facilitate the utility of model-integrated evidence to support demonstrations of bioequivalence
- Expand the use of artificial intelligence and machine learning tools

FY2025 GDUFA Science and Research Projects

- 30 ongoing grants and 34 ongoing contracts
- 64 external research collaborations
- 51 intramural GDUFA science projects
- 39 peer-reviewed articles
- 12 public scientific meetings, webinars, trainings, and workshops, reaching more than 12,500 participants worldwide

Comparative Use Human Factor Study – Drug Device Combination Product Evaluation

FDA gathers data on the impact of the three “other design differences”

Support generic development of GLP-1s and other pen injector products

Gain firsthand experience with the challenges of designing and conducting a CUHF study to better inform updated guidance to industry

Industry learns from precedents FDA sets

- Methodology
- Recruiting strategy
- SAP
- Data analysis

Publish data (e.g., base error rates) in the public domain to support future submissions (e.g., determining sample size)

Collaborations

Global Affairs Program

PROACTIVE INFORMATION SHARING

CASE DRIVEN DISCUSSIONS

STREAMLINING GENERIC DEVELOPMENT

Patient Engagement

Public meetings to solicit input on research priorities, user fee negotiations, and more

Funds **research grants** that investigate specific views and concerns from the patient perspective

Encourages **integrating patient input** into generic drug development and decision-making

Quality

The State of Pharmaceutical Quality

ANDA Manufacturing

- ANDAs in CDER catalog up 4.4% (to 14,168), but ANDA Field Alert Reports (FARs) down 8.7%
- U.S. (48%) and India (41%) were top sources of sites responsible for recalls

API Supply Chain

- 25% of import alerts were for API manufacturers (up from 2% in FY2023)
- 72% of enforcement actions for API manufacturers over 5 years were for sites supplying only compounding pharmacies

Regulatory Tools & Oversight

- Foreign inspection: 34% of India, 28% of China
- § 704(a)(4) record requests drove >60% of import alerts

Sources:
FY2023 FDA Report on the State of Pharmaceutical Quality
FY2024 FDA Report on the State of Pharmaceutical Quality

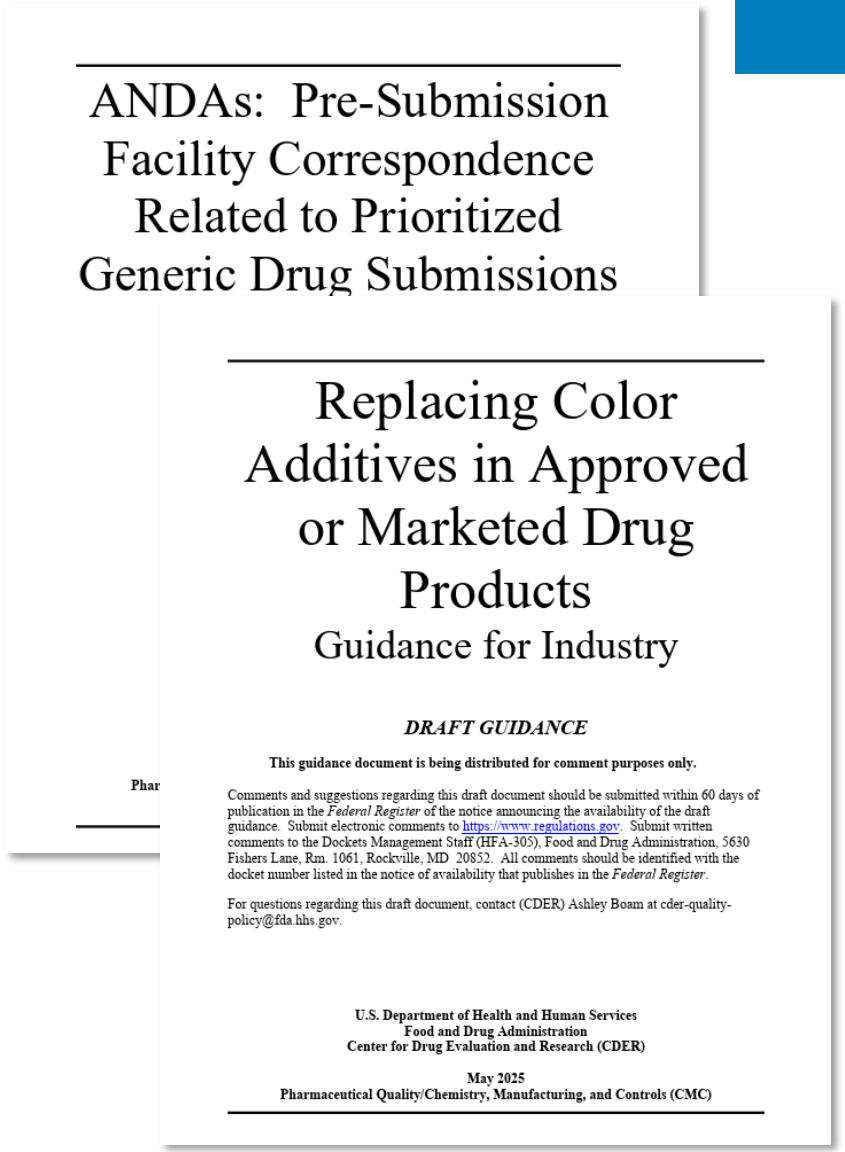
Recent Quality Guidance

Final Guidance: Pre-Submission Facility Correspondence Related to Prioritized Generic Drug Submissions

- Complete PFCs enable 8-month priority review eligibility
- Allows early facility assessment before ANDA submission

Draft Guidance: Replacing Color Additives in Approved or Marketed Drug Products

- Recommendations for replacing color additives via CBE-30 supplements
- FD&C Red No. 3 phase-out deadline: January 18, 2028



ANDAs: Pre-Submission Facility Correspondence Related to Prioritized Generic Drug Submissions

Replacing Color Additives in Approved or Marketed Drug Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Ashley Boam at cder-quality-policy@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2025
Pharmaceutical Quality/Chemistry, Manufacturing, and Controls (CMC)

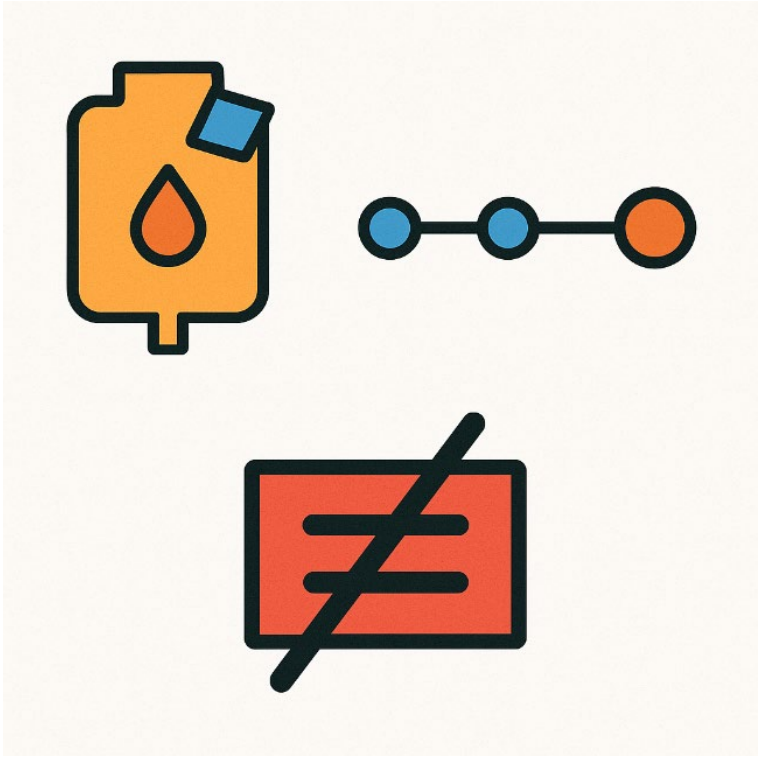
Nitrosamine Updates

Leachable Nitrosamines: New Contamination Source

- Identified in infusion bag packaging (printed overwraps, pouches with inks/nitrocellulose)
- Conduct risk assessments and test; report results for approved products by November 16, 2025

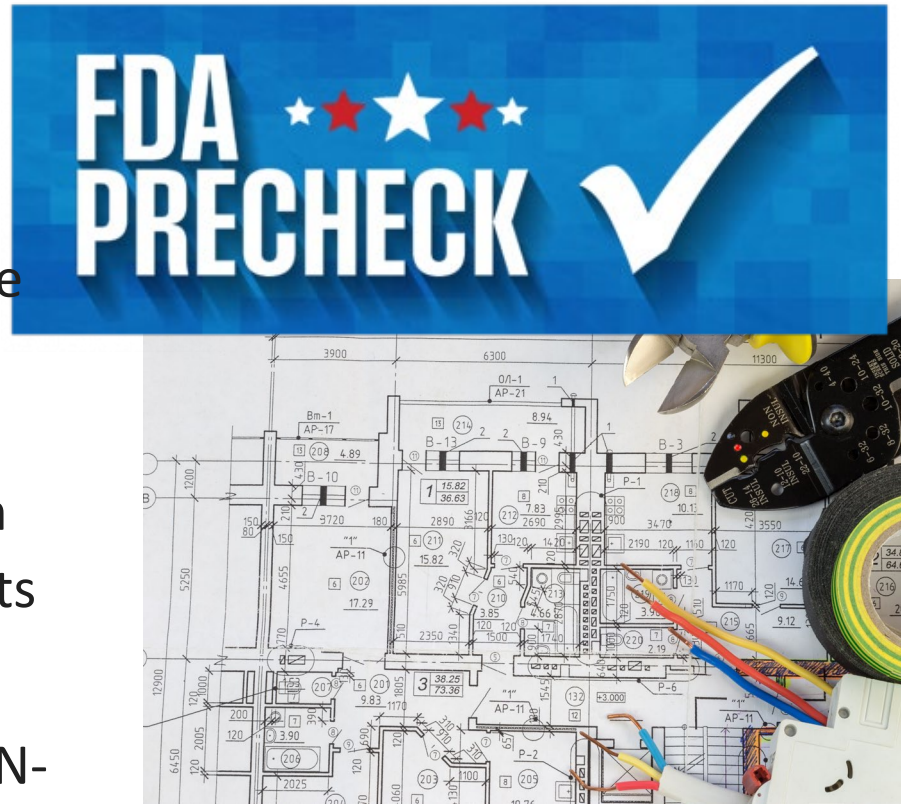
Nitrosamine Drug Substance-Related Impurities (NDSRI) Timeline Extension with Enhanced Accountability

- August 1, 2025 deadline extended; submit comprehensive progress updates as soon as possible
- FDA analyzing industry data to establish revised timelines



Introducing FDA PreCheck

A Two-Phase Approach to Accelerate Domestic Pharmaceutical Manufacturing



Phase 1 - Facility Readiness

- Early FDA engagement during facility design and construction
- Facility-specific Drug Master File submission (Type V) before operations begin

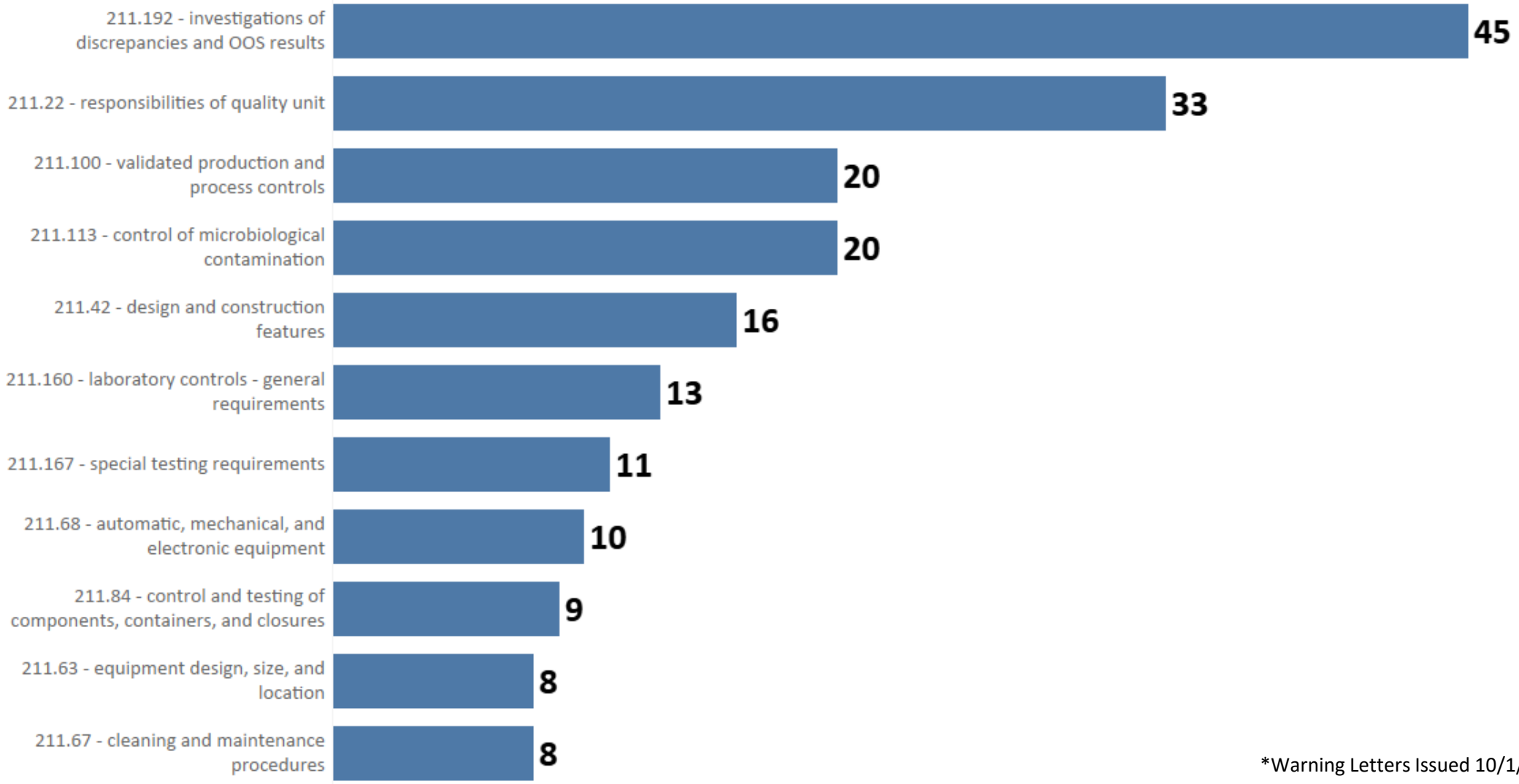
Phase 2 - Application Submission

- Streamlined review process building on Phase 1 foundation
- Pre-submission meetings and expedited quality assessments

Public Comments

- Electronic submissions: regulations.gov (Docket FDA-2025-N-2489)
- Comments due October 30, 2025

Top CGMP Warning Letters Citations to Rx(Primarily Generic) Finished Dosage Manufacturers



*Warning Letters Issued 10/1/2019 to 7/31/2025

Current CGMP Compliance Trends for Generics

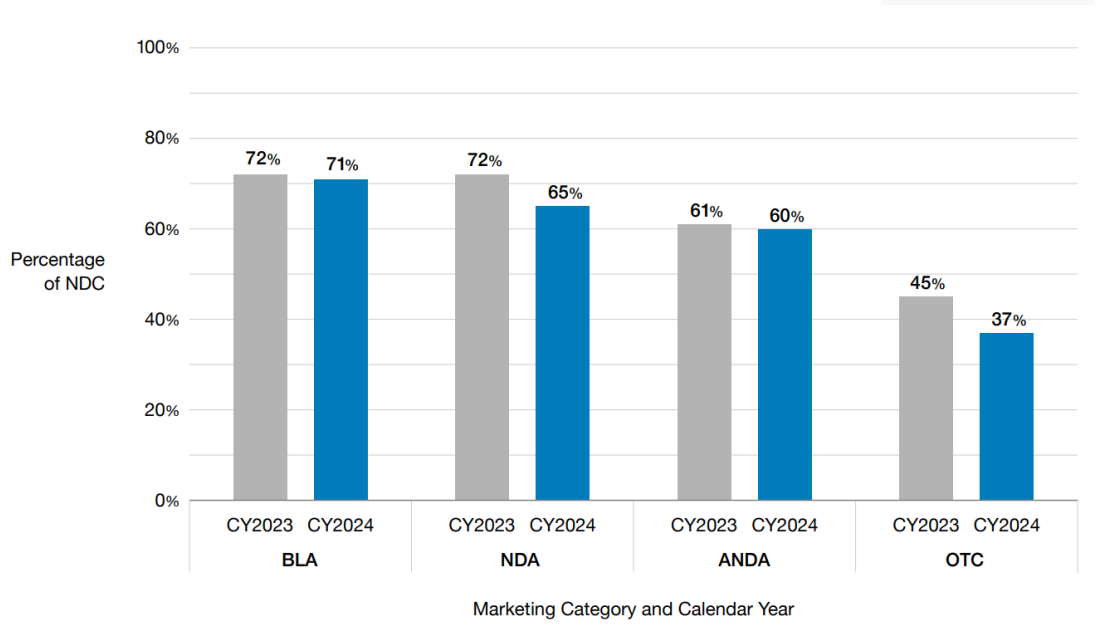
- **Inadequate Control of Particulates in Injectables**
  - Excessive levels of intrinsic particles
  - Improper minimization of risk when extrinsic particles discovered
- **Inadequate Operations for Aseptically Filled Drug Products**
  - Improper personnel behavior in the aseptic core
  - Inadequate environmental monitoring oversight
- **Ongoing Concerns with Dissolution of Modified Release Oral Drug Products.**
  - Improper stage 2/3 testing
  - Inadequate investigations into dissolution failures to determine root cause

Drug Shortages

The Challenge: Supply Chain Vulnerability

Understanding availability risks starts and ends with good data

- FDA needs manufacturers' amount reporting

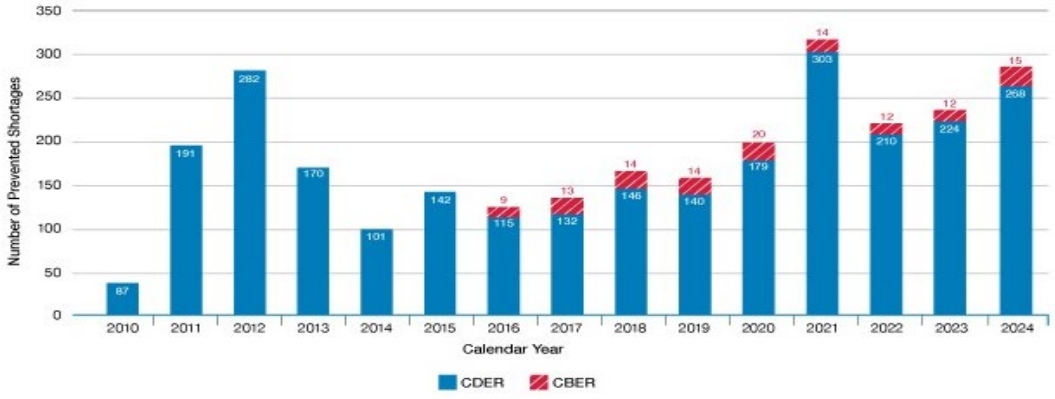


Sources:
FY2024 FDA Report on the State of Pharmaceutical Quality

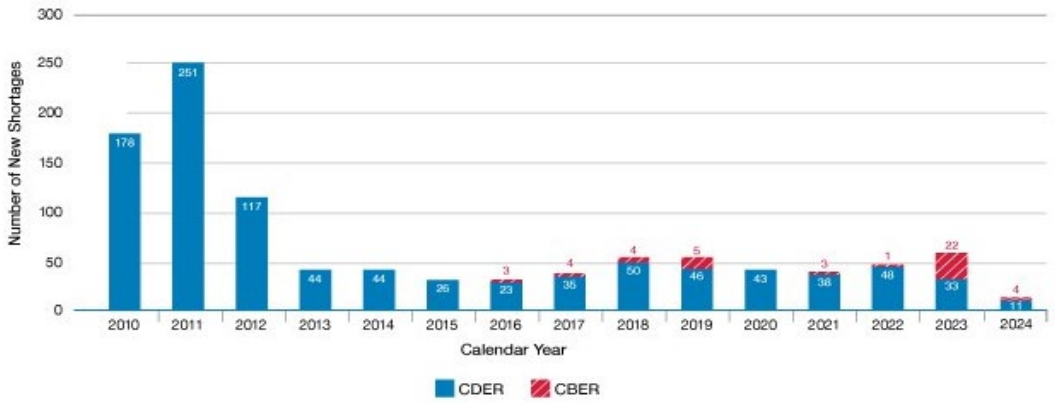
Drug Shortage Successful Efforts

- Through ongoing dialogue/work with industry the number of prevented shortages continues to be significant.
- 2024 showed fewest number of new shortages since tracking began – 11 new shortages reported

Prevented Shortages



New Shortages



2024: CDER New Shortages 11, CDER Prevented Shortages 268

Additional CY 2024 Stats

Breakdown of CDER's and CBER's Shortage Numbers for CY 2024

	CDER	CBER
NUMBER OF SHORTAGES		
New Shortages	11	4
Prevented Shortages	268	15
Ongoing Shortages	88	25
Notifications	1420	39
Number of Manufacturers Notifying	129	28
ACTIONS TAKEN TO MITIGATE SHORTAGES		
Regulatory Flexibility and Discretion	106	1
Expedited Reviews	206	19*
Expedited Inspections	20	0

Breakdown of Expedited Reviews in CY 2024 by Submission Type

Submission Type	Expedited Reviews
NDA/NDA Supplements (CDER)	47
ANDA/ANDA Supplements (CDER)	149
BLA/BLA Supplements (CDER)	10
BLA/BLA Supplements (CBER)	6*

Drug Shortage Prevention and Mitigation

Early Notification to the Drug Shortage Staff (DSS) is critical.

Provide short- and long-term plans for preventing and addressing shortages while maintaining and improving quality

Work with FDA to minimize shutdowns or slowdowns that could lead to shortages

Contact DSS at Drugshortages@fda.hhs.gov or Report through the CDER Nexgen Portal

Driving Access

Improved Submissions

GDUFA Enhancements

Innovative Efforts

Looking to the Future

Participate in Our Upcoming Events

- FDA and Center for Research on Complex Generics (CRCG) collaborations: www.complexgenerics.org
- OGD and CDER Small Business & Industry Assistance (SBIA) collaborations: https://sbiaevents.com

2025

Nov 19-20: **Visionary Standards**: Advancing Science and Regulation in Generic Ophthalmic Products
FDA/CRCG Workshop

Dec 11: **Quality and Regulatory Predictability**: Shaping USP Standards
FDA/SBIA Webinar

Participate in Our Upcoming Events (2)

2026

Apr 22-23: **Generic Drug Forum**
FDA Workshop

May 05-06: **Bioequivalence Innovations for Oral Generic Products**: Biowaivers, Bridging, and Generic Development for Oncology and Discontinued Products
FDA/CRCG Workshop

Jun 08-09: **Fiscal Year 2026 Generic Drug Science and Research Initiatives**
FDA Public Workshop

Sep 23-24: **Navigating the GLP-1 Generic Pathway**: From Peptide to Patient
FDA/CRCG Workshop

Oct 14-15: **Advancing Bioequivalence Frameworks for Inhalation & Nasal Drug Products**: Optimizing In Vitro, In Vivo, and In Silico Methods
FDA/CRCG Workshop

Dec 01-02: **Long-Acting Injectable (LAI) Generics**: Navigating Technical Hurdles in Product Development and Regulatory Assessment
FDA/CRCG Workshop

Stay Informed

- **Your Regulatory Project Manager is your best source of information on your ANDA**

- **Follow our public communications**
  - ❖https://www.fda.gov/about-fda/contact-fda/get-email-updates
    ("Generic Drugs Updates" and more)

43


FDA
U.S. FOOD & DRUG
ADMINISTRATION