Overview of the FDA Product-Specific Guidance (PSG) Program

Generic Drug Forum - April 10, 2024

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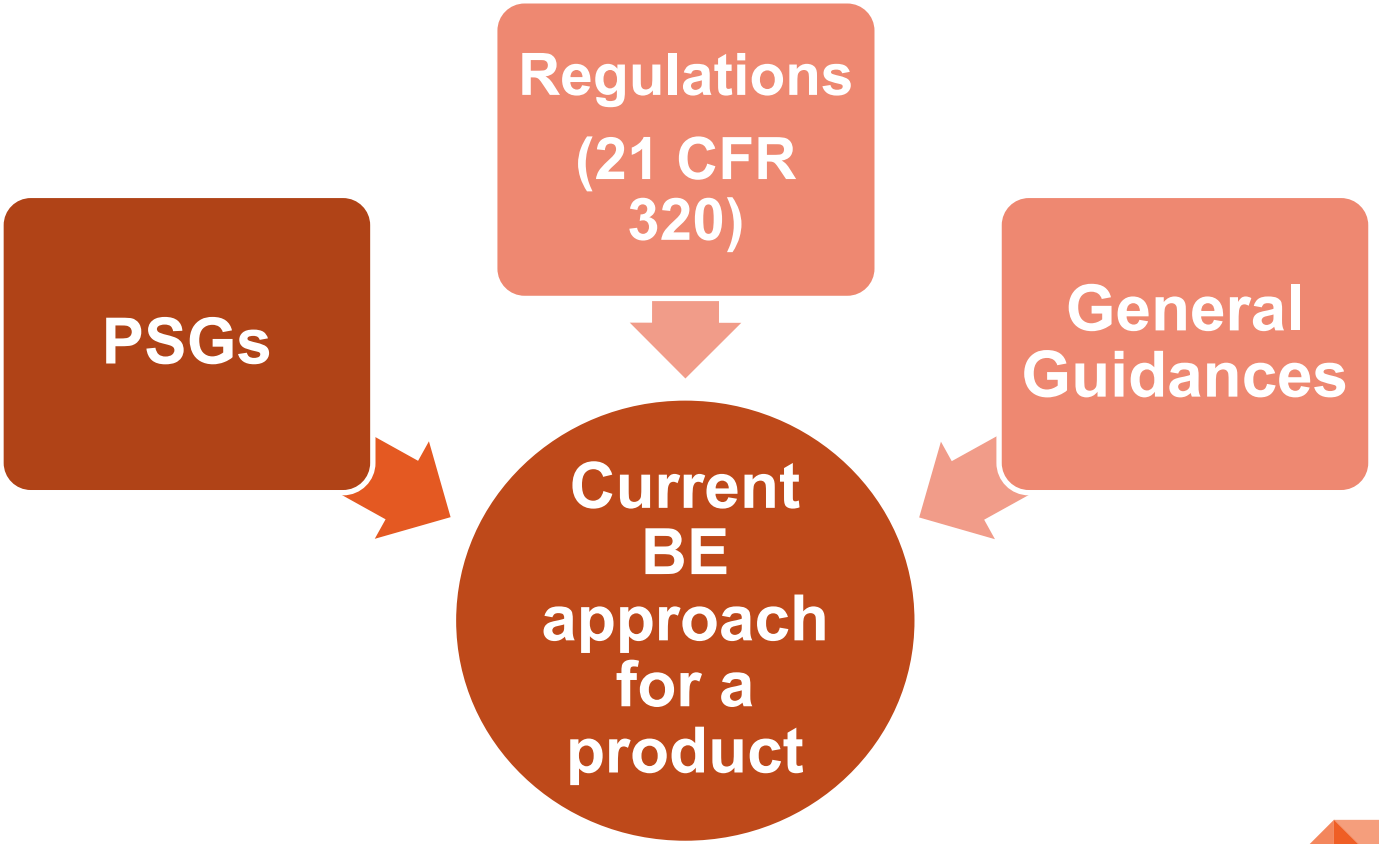
Outline

- Product-Specific Guidance (PSG) background and relation to FDA's Abbreviated New Drug Application (ANDA) program
- Overview of the FDA PSG program, GDUFA III commitments, and public comments/requests
- GDUFA III PSG teleconferences (T-Cons) and PSG meetings

What is a Product-Specific Guidance (PSG)?

- Reflects FDA's current thinking and expectations on how to develop a generic drug product therapeutically equivalent to a specific reference listed drug (RLD)
- Contains product-specific recommendations
  - Identifying the methodology for developing generic drugs and generating evidence recommended to support ANDA approval
  - Including key science and research output
- Unique to the generic drug development program

ANDA: Abbreviated New Drug Application


Regulations (21 CFR 320)
PSGs
General Guidances
Current BE approach for a product

PSG is an Integral Part of the FDA's ANDA Program

Pre-ANDA Program

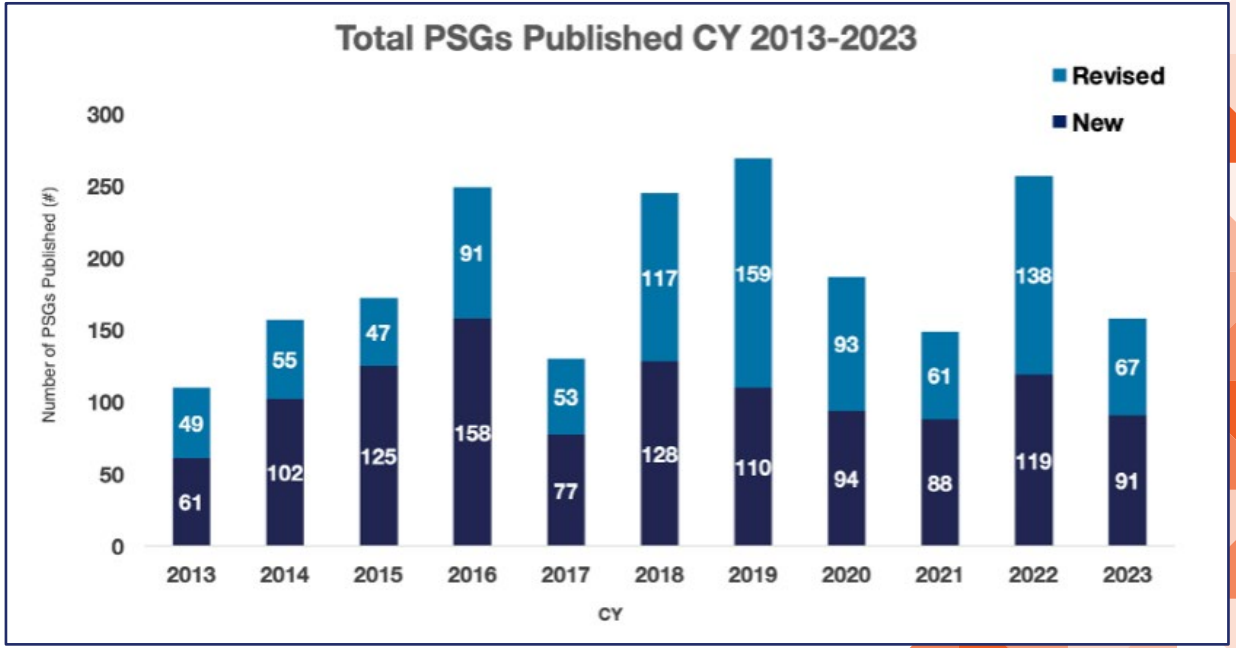
- Pre-ANDA Meetings
- Product-Specific Guidances (PSGs)
- Controlled Correspondences

GDUFA: Generic Drug User Fee Amendments

Background on PSGs

- Started in 2007, FDA has published PSGs to provide clear and direct recommendations to ANDA applicants

- 2,186 PSGs on the FDA PSG webpage as of April 2024
  - ~40% for complex products



https://www.fda.gov/drugs/guidances-drugs/product-specific-guidances-generic-drug-development

GDUFA III Commitment on PSG Development

- For **Non-Complex NCE New Drug Applications** (**NDAs**) approved on or after October 1, 2022, a PSG will be issued for 90% of such NDA products within 2 years after the date of approval.
  - No change from GDUFA II

- For **Complex Products** approved in NDAs on or after October 1, 2022, a PSG will be issued for 50% of such NDA products within 2 years after the date of approval, and for 75% of such NDA products within 3 years after the date of approval.

- FDA will continue to develop PSGs for **Complex Products** approved prior to October 1, 2022, for which no PSG has been published.

GDUFA: Generic Drug User Fee Amendments; NCE: New Chemical Entity; NDA: New Drug Application; GDUFA III Commitment Letter

PSG Process

Quarterly Batch/
Standalone

PSG Prioritization and Development

Initiating Events

- Recently approved NDAs and supplemental NDAs
- FDA analysis of products without PSGs
- Pre-ANDA meetings
- Public requests
- Comments submitted to PSG docket
- Controlled correspondences
- Citizen petitions

Prioritization

- GDUFA commitments
- Stakeholder interest in ANDA submission
- Drug availability and accessibility
- Public requests from generic drug industry and other stakeholders
- Public health priorities

Data to Support PSG Development

- Pharmacokinetic (PK) and pharmacodynamic (PD) modeling
- Previous BE studies
- NDA review and labeling
- Pharmacovigilance
- GDUFA-funded research outcomes

PSG Snapshot: *www.fda.gov/media/150142/download?attachment*

How are Revised PSGs Planned?

Identification of Needs for PSG Revision

- Changes to the RLD: e.g., labeling update, supplements, new strength
- Newly identified safety concerns
- Consistency with revision to general guidances
- Responses to the received BE comments
- Citizen petitions
- New BE approaches from research: e.g., addition of the in vitro option
- New knowledge from ANDA assessments, Pre-ANDA meetings and controlled correspondences

Notification of PSG Revision*

Category	Description
Critical	PSG revision includes additional bioequivalence studies or evidence recommended to support FDA approval that reflect a change in the safety or effectiveness of the drug product. The critical revision has a potential impact on all ANDAs including the approved applications.
In Vivo Major	PSG revision includes additional in vivo bioequivalence studies or evidence recommended that is necessary to establish BE and support FDA approval
In Vitro Major	PSG revision includes additional in vitro bioequivalence studies or evidence recommended that is necessary to establish BE and support FDA approval
Minor	PSG revision includes in vivo and/or in vitro changes that is not considered critical or major
Editorial	PSG revision includes non-substantive changes

*Upcoming PSGs for Generic Drug Product Development

When are PSGs published?

- New and revised PSGs are published quarterly in four batches a year
  - February, May, August, and November
- A PSG may be published as a stand-alone guidance or a stand-alone batch outside the quarterly batches, e.g.,
  - Coordinate with citizen petition responses
  - Meet the GDUFA goal date
  - Efficiency in developing PSGs for products in the same class
  - Level 2 Revision(s)
- The FDA will issue a notice in the Federal Register for every batch and stand-alone posting, except Level 2 Revisions

What is a Level 2 PSG Revision?

- **Level 1** guidance documents set forth the Agency's initial interpretations of statutory or regulatory requirements; describe changes in FDA's earlier interpretation or policy that are of more than a minor nature; and deal with complex scientific or highly controversial issues.
- **Level 2** guidance documents address existing practices or minor changes in FDA's interpretation or policy.
- Level 2 PSG Revisions
  - Typographical errors found in PSGs
  - No change in BE recommendation or Agency thinking
  - For example, three level 2 PSG Revisions published in Nov 2023

Upcoming PSGs for Generic Drug Product Development (Forecast List)

- Describes the FDA's plans for all upcoming new and revised PSGs of generic drug products in the next 12 months
  - **New in GDUFA III:** The forecast list includes both complex and non-complex products
- Enhances transparency in PSG development or revision plan for generic drug products
  - **New in GDUFA III:** Updates include projected PSG publication dates in MM/YYYY or descriptive timeline (within or beyond 12 months)
- Ensure consistency in FDA recommendations/decisions following previous iterations of the PSG and establish principles for PSG revisions to reflect "most accurate, sensitive, and reproducible" approaches
  - **New in GDUFA III:** Redefine revision classification (category with description)
- Updated quarterly with each PSG batch posting

Upcoming PSGs for Generic Drug Product Development (Forecast List)

Planned New PSGs for Complex and Non-Complex Generic Drug Products
Updated February 15, 2024

Active Ingredient(s)	Route of Administration	Dosage Form	RLD or RS Application Number	Product Complexity	Planned Publication
Air Polymer-Type A	Intrauterine	Foam	212279	Complex	08/2024
Amikacin Sulfate	Inhalation	Suspension, Liposomal	207356	Complex	05/2024
Aripiprazole	Oral	Tablet	207202	Complex	Within the next 12 months
Atorvastatin Calcium	Oral	Suspension	213260	Non-Complex	05/2024
Baclofen	Oral	Suspension	215602	Non-Complex	05/2024
Bexagliflozin	Oral	Tablet	214373	Non-Complex	05/2024
Clobetasol Propionate	Topical	Cream	209483	Complex	Beyond 12 months
Daprodustat	Oral	Tablet	216951	Non-Complex	05/2024
Desmopressin Acetate	Nasal	Spray, Metered	201656	Complex	11/2024
Elacestrant Dihydrochloride	Oral	Tablet	217639	Non-Complex	05/2024

Planned Revised PSGs for Complex and Non-Complex Generic Drug Products
Updated February 15, 2024

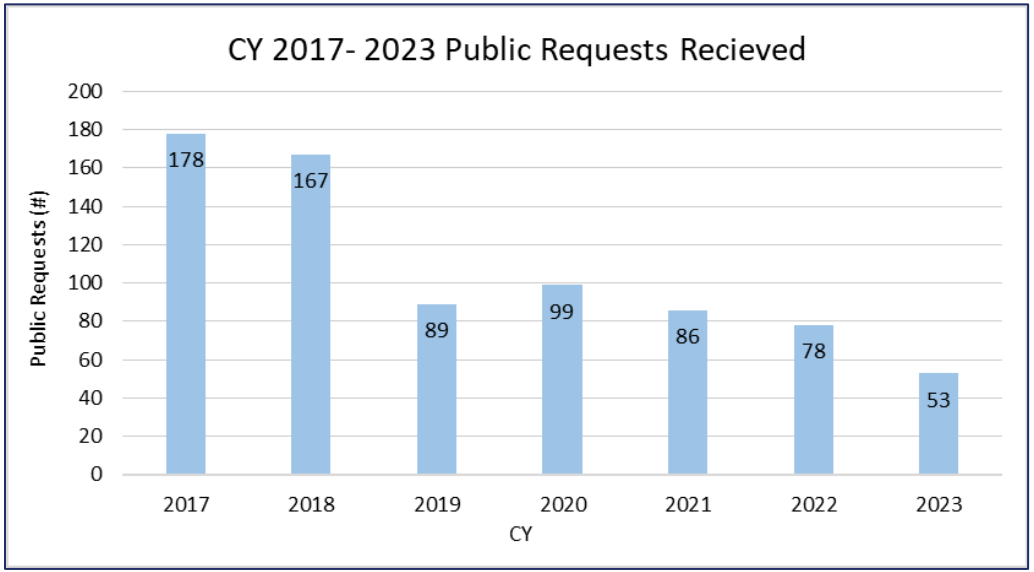
Active Ingredient(s)	Route of Administration	Dosage Form	RLD or RS Application Number	Planned Revision Category with Description	Product Complexity	Planned Publication
Acetaminophen; Butalbital	Oral	Capsule	088831	Minor Revision: Remove recommendation on a strength due to safety concerns	Non-Complex	Within the next 12 months
Albuterol Sulfate	Inhalation	Aerosol, Metered	020503, 020983, 021457	Editorial Revision: Update the language Minor Revision: Clarify in vitro study design; Revise recommendations for device comparisons	Complex	08/2024
Albuterol Sulfate; Ipratropium Bromide	Inhalation	Spray, Metered	021747	Editorial Revision: Update the language Minor Revision: Clarify in vitro study design; Revise recommendations for device comparisons	Complex	08/2024
Allopurinol	Oral	Tablet	016084	Minor Revision: Add information on newly approved (lower or middle) strengths of the RLD/RS	Non-Complex	08/2024

Public Comments on PSGs

- FDA issues a Federal Register Notice announcing the availability of new and revised PSGs via Docket Number FDA-2007-D-0369
- The notice will identify a comment period for the draft recommendations
  - Comment can be submitted electronically to the docket or by mail
  - Users can request additional assistance with a Help Desk ticket: https://www.regulations.gov/support
- FDA will consider comments on draft PSGs while revising the PSGs

Public Requests for PSGs

- Public requests for PSGs can be submitted using the CDER Direct NextGen Collaboration Portal
  - FDA reviews requests and takes appropriate action



PSGs Withdrawn

CDER Product-Specific Guidances Withdrawn Listing
Updated April 10th, 2023

Active Ingredient	Type of Guidance	Route and Dosage Form	RLD	Date PSG Posted or Revised	Federal Register Notice / Withdrawal Date
BUTENAFINE HYDROCHLORIDE	Draft	Topical Cream	021408	03/01/2012	02/01/2015
HYDROXYPROGESTERONE CAPROATE	Draft	Subcutaneous Solution	021945	09/16/2019	04/06/2023
LEVONORGESTREL	Draft	Intrauterine Device	203159	04/01/2014	10/01/2014
LORCASERIN HYDROCHLORIDE	Draft	Oral Tablet, Extended Release	022529	03/01/2015	03/04/2021
LORCASERIN HYDROCHLORIDE	Draft	Oral Tablet, Extended Release	208524	05/01/2017	03/04/2021
LOVASTATIN; NIACIN	Draft	Oral Tablet, Extended Release	021249	07/01/2009	04/18/2016
NIACIN; SIMVASTATIN	Draft	Oral Tablet, Extended Release	022078	10/01/2011	04/18/2016

Note: If a PSG is re-posted, it will be removed from the withdrawn list

- Recommendations in a PSG are withdrawn when they no longer reflect the FDA's current thinking
- Withdrawn PSGs could also be due to a withdrawn RLD for safety or efficacy reasons
  - List of withdrawn PSGs can be accessed: https://www.fda.gov/media/90032/download

PSG T-Cons

- ANDA applicant(s) can request a PSG T-con at any time during their product development (pre-submission or post-submission) when FDA publishes a new or revised guidance that introduces or revises a recommendation if:
  - Recommendation is related to an in vivo BE study
  - ANDA applicant has already commenced an in vivo BE study that may be different from PSG recommendations as of the published date for the new or revised PSG
- A prospective ANDA applicant should submit a request for a pre-submission PSG T-con or pre-submission PSG meeting electronically through the CDER Direct NextGen Collaboration Portal
- An ANDA applicant should submit a request for a post-submission PSG T-con or post-submission PSG meeting electronically through the Electronic Submissions Gateway
- In FY 2023, two PSG T-con requests were received and held.

Draft Guidance for Industry on PSG T-cons and Meetings: www.fda.gov/media/165468/download

PSG Meetings

- PSG meetings (pre-submission or post-submission) can be requested following the PSG T-cons if additional discussion is needed
  - Allows a forum to discuss the scientific rationale for an approach other than the approach recommended in the PSG
    - Pre-submission PSG meetings can be requested if the ANDA has not been submitted
    - Post-submission PSG meetings can be requested if the ANDA has been submitted
- Controlled correspondence is an alternative way for applicants to follow up with FDA on the remaining issues following the PSG T-con
- Other pre-ANDA and ANDA scientific meetings are available as alternative to PSG meetings
  - FDA recommends that applicants not submit a controlled correspondence and a request for a meeting at or around the same time with the same or similar questions
- In FY 2023, FDA did not receive PSG meeting request

Draft Guidance for Industry on PSG T-cons and Meetings: www.fda.gov/media/165468/download

Upcoming SBIA Webinar on PSGs

"Facilitating Generic Drug Product Development through Product-Specific Guidances"

- **Date:** April 25, 2024, 1-4 PM EDT
- **Topics covered:**
  - **PSG Program: Updates and Overview of Available Resources**
  - **Beyond General Guidance: Tailored PSG Recommendations for Immediate Release Oral Drug Products**
  - **Biopharmaceutics Classification System Waiver Option in PSGs**
  - **Development of Generic Drug Products Under Suitability Petition**
  - **Device and User Interface Assessment Recommendations in Drug-Device Combination Product PSGs**
  - **Consideration Factors for Study Population Selection in Bioequivalence Studies with Pharmacokinetic Endpoints**
  - **FDA Dissolution Methods and Navigating the Dissolution Database**

Challenge Question 1

What is **NOT** one of the factors FDA takes into consideration while prioritizing PSG development or revision?

a) ANDA assessment goal dates

b) Public health priorities

c) Public requests

d) Drug availability and accessibility

Challenge Question 2

What is a new feature added with GDUFA III commitments for the "Upcoming PSGs for Generic Drug Product Development," otherwise known as the "PSG Forecast List"?

a) Forecasting both New and Revised PSGs

b) Forecasting both Non-Complex and Complex PSGs

c) Forecasting specific Revision Reasons for Revised PSGs

d) Updated quarterly with each PSG batch posting

Resources

- Product-Specific Guidances for Generic Drug Development: https://www.fda.gov/drugs/guidances-drugs/product-specific-guidances-generic-drug-development
- GDUFA III Commitment Letter
- MAPP 5240.10: Classifying Approved New Drug Products as Complex Products for Generic Drug Development Purposes (April 2022)
- Product-Specific Guidances for Generic Drug Development (*PSG Database*): https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm
- GDUFA III Enhancement to the Pre-ANDA Program: https://www.fda.gov/industry/generic-drug-user-fee-amendments/gdufa-iii-enhancements-pre-anda-program
- Draft Guidance for Industry: Product-Specific Guidance Meetings Between FDA and ANDA Applicants Under GDUFA (February 2023)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