Suitability Petitions

An Avenue for Patient-centric Formulations

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Learning Objectives

- Understand the use, purpose, and GDUFA III commitments for Suitability Petitions
- Understand Suitability Petition assessment and case studies for patient-centric dosage form changes
- Provide Suitability Petition tips, best practices, and preparation for future ANDAs

What is a Suitability Petition?

A request to submit an abbreviated new drug application (ANDA) that is different from the reference listed drug (RLD) in one or more of the following:

- Strength
- Route of administration
- Dosage form
- Change in one active ingredient in a fixed-combination drug product (i.e., a drug product with multiple active ingredients)

Significance of Suitability Petitions

- Allows the generic drug industry to fill market demands or opportunities without the need for new clinical data
  - Dosing convenience for patients (e.g., no tablet splitting with new strengths, eliminating the need to take multiple tablets to achieve a desired dose, **ease of swallowing with new dosage forms**)
  - Efficiency of dosing for health care providers
  - Reduction of pharmaceutical waste

- Maximizes the 505(j)-application process
  - No unnecessary human studies
  - Efficient FDA review process
  - Allows resources to focus on drug development of new therapeutics versus modifications to already approved drug products

Suitability Petitions and PREA

- Suitability petitions proposing a change in **dosage form**, **route of administration**, **or** for **a change in active ingredient in a fixed-combination drug** trigger the requirement for pediatric assessments or molecularly targeted pediatric cancer investigations under PREA
- Petitioners must submit a waiver request to waive these requirements
- PREA authorizes FDA to waive the requirement to submit a pediatric assessment, based on established criteria, for some or all pediatric age groups
- For information on PREA requirements and requesting a waiver, refer to Draft Guidance for Industry: Pediatric Drug Development: Regulatory Considerations — Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act May 2023

Requesting a PREA Waiver

To request a waiver, petitioners should provide the following:

- Petitioner name, drug name, and indication
- The age group(s) included in the waiver request
- The statutory reason(s) for requesting a waiver, including reference to the applicable statutory authority[1]
- Evidence that the request meets the statutory reason(s) for waiver
- All relevant scientific/clinical justifications for the waiver request should be included

[1] See section 505B(a)(5) of the FD&C Act (21 U.S.C. 355c(a)(5))

Reasons for Denial of a Suitability Petition

FDA will approve a suitability petition unless, among other reasons, one of the following is applicable (see 21 CFR 314.93(e)(1)(i)-(vi)):

- Investigations must be conducted
- A drug product is approved in an NDA for the change described in the petition
- Triggers the need for pediatric studies under the Pediatric Research Equity Act (PREA) and the waiver request has been denied
- The proposed change from the RLD is not one of the permitted types of changes outlined in 21 CFR 314.93(b)
- Significant labeling changes are necessary
- RLD has been withdrawn from sale for safety or effectiveness (S/E) reasons or RLD has been voluntarily withdrawn from sale and the Agency has not made an S/E determination

SUITABILITY PETITIONS IN GDUFA III

GDUFA III Commitment	Outcome
In FY 2024, 50 percent of submissions within 6 months after completeness assessment, up to a maximum of 50 suitability petitions completed	99/103 on time (96%)
In FY 2025, 70 percent of submissions within 6 months after completeness assessment, up to a maximum of 70 suitability petitions completed	94/94 on time (100%)
In FY 2026, 80 percent of submissions within 6 months after completeness assessment, up to a maximum of 80 suitability petitions completed	N/A
In FY 2027, 90 percent of submissions within 6 months after completeness assessment, up to a maximum of 90 suitability petitions completed	N/A

GDUFA III Petitions

Changes Proposed in Suitability Petitions

Type of Change	Petitions Submitted (FY24 and FY25)
Strength	128 (63%)
Dosage Form	47 (23%)
Strength & Dosage Form	24 (12%)
Route of Administration	2 (1%)
Other (Non-petitionable Changes)	2 (1%)
Total	203

GDUFA III Petitions (continued)

Final determinations:

	FY '24	FY '25
Substantive responses issued	103	94
Approved	48	55
Denied	52	36
• Already approved NDA product	8	2
• Non-petitionable change proposed	2	1
• No S/E determination for discontinued RLD	2	2
• **PREA waiver denied***	17	9
• Other (clinical trials or significant labeling changes necessary)	23	22
Partial Grant/Partial Denial	3	3
Withdrawn (by petitioner or administratively by OGD)	3	2

*37% of all dosage form/route of administration changes denied by PERC

SUITABILITY PETITION ASSESSMENT

Assessment Approach and Resources

- Suitability Petition
  - Proposed change, petitioner rationale
- RLD Labeling
  - Dosage & Administration, Special Populations, Warnings/Precautions, Clinical Pharmacology
- Proposed Labeling
  - How does labeling differ from RLD labeling?

Does it fail any criteria established in 21 CFR 314.93(e)(1)(i)-(vi))?

Assessment Approach

- Strength Changes
  - Review of all RLD indications and dosing
  - 75% of GDUFA III petitions
- **Dosage Form Changes**
  - Past precedent for allowing change
  - Maintain same dosing instructions as RLD
  - Modified administration instructions
  - **Patient-centric changes**
    - Orally disintegrating tablets (>50% of dosage form change)
    - Liquid oral dosage forms

Assessment Approach: Proposed Labeling

- How does proposed change(s) affect current RLD labeling?
  - **How Supplied** or **Dosage Forms and Strengths** changes only?
  - New **administration** or **preparation** instructions, including Instructions for Use (IFU)?
  - New **dosing information** or instructions?
  - New **warning** to safely use product needed?
- Must consider if changes to labeling will be needed, compared to RLD, and if such changes are allowable under a future ANDA
- Note: This is NOT a complete labeling assessment
- Labeling changes to **How Supplied** or **Dosage Forms and Strengths** generally permissible
- Labeling changes in ANDAs **are generally permissible** for additional **administration instructions** to describe how to use the proposed product

Orally Disintegrating Tablet (ODT) Changes

- Most common dosage form change under GDUFA III
- Precedent for ODT petition approvals
- Precedent for ANDA approval citing approved petition
  - Carbidopa/Levodopa 10mg/100mg, 25mg/100mg, 25mg/250mg (RLD Sinemet N017555)
  - Petition for ODT change approved 8/29/2002 (#02P-0033/CP1)
  - 4 approved ODT Carbidopa/Levodopa products in Orange Book
- Approved ODTs under 505(b)(2) have relied only on BE testing
- ODTs not intended to be split, potential concern if RLD tablet scored with split tablet dosing

Patient-centric Liquid Dosage Forms

FDA-2024-P-0422 Folic Acid Oral Solution, 0.1 mg/mL and 1 mg/mL

- RLD Folic Acid Tablets, 1 mg (ANDA 080680)
- Change in dosage form and strength
- Indicated for megaloblastic anemias and anemias of nutritional origin, pregnancy, infancy or childhood
- Assessment (approval)
  - All recommended doses can be achieved using the proposed solution
  - Proposed changes should not raise questions of safety or efficacy because the uses and indications of the proposed drug products are the same as RLD
  - PREA waiver granted
  - Bioequivalence will be evaluated during future ANDA submission

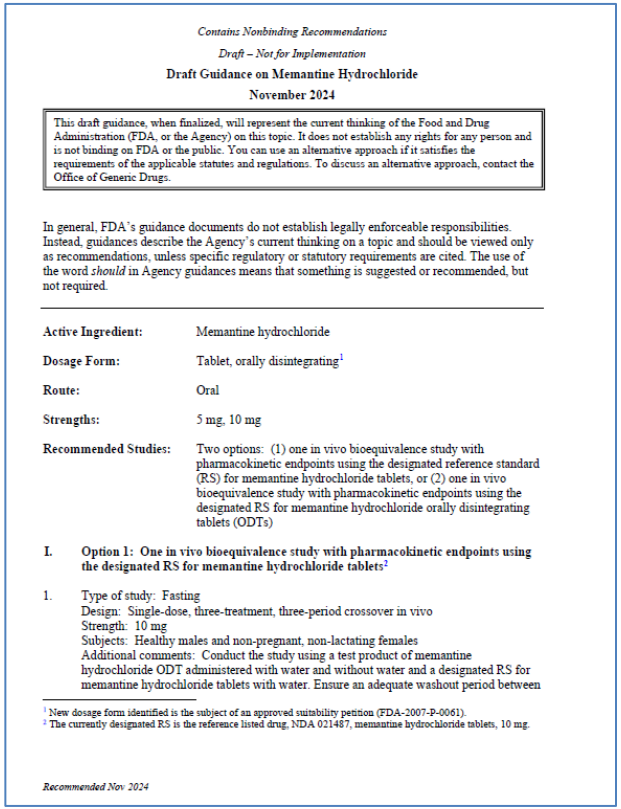
Patient-centric Dosage Forms

FDA-2025-P-1026 Linezolid Tablets for Suspension, 600 mg

- RLD Zyvox (Linezolid) Tablets, 600 mg
- Change in dosage form
- Antibacterial indicated for multiple infection types
- Assessment (approval)
  - Product involves dispersion of linezolid tablets into an oral suspension suitable for pediatric or adult patients with swallowing difficulties
  - For administration it can disintegrate in mouth or placed in a small volume of liquid
  - Proposed changes should not raise questions of safety or efficacy because the uses and indications of the proposed drug products are the same as RLD
  - PREA waiver granted
  - Future labeling should address proper dosage and administration instructions to mitigate wrong technique
  - Bioequivalence will be evaluated during future ANDA submission

Suitability Petition Tips and Best Practices

- Any ANDA applicant can reference an approved suitability petition
- All petitions available at regulations.gov
- Bioequivalence recommendations may be available on the Product Specific Guidance (PSG)
- Submit controlled correspondences (CCs) for product development advice for future petitioned ANDA



Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Memantine Hydrochloride

November 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient:	Memantine hydrochloride
Dosage Form:	Tablet, orally disintegrating[1]
Route:	Oral
Strengths:	5 mg, 10 mg
Recommended Studies:	Two options: (1) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated reference standard (RS) for memantine hydrochloride tablets, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for memantine hydrochloride orally disintegrating tablets (ODTs)

I. Option 1: One in vivo bioequivalence study with pharmacokinetic endpoints using the designated RS for memantine hydrochloride tablets[2]

1. Type of study: Fasting
   Design: Single-dose, three-treatment, three-period crossover in vivo
   Strength: 10 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Conduct the study using a test product of memantine hydrochloride ODT administered with water and without water and a designated RS for memantine hydrochloride tablets with water. Ensure an adequate washout period between

[1] New dosage form identified is the subject of an approved suitability petition (FDA-2007-P-0061).
[2] The currently designated RS is the reference listed drug, NDA 021487, memantine hydrochloride tablets, 10 mg.

Recommended Nov 2024

Reminders about future ANDAs

<u>All petitioned ANDAs</u>

- Adequate BE testing required
- If approved, will not be therapeutically equivalent to RLD

<u>Patient-Centric Dosage form changes</u>

- ANDA labeling should describe administration instructions
- Appropriate BE testing corresponds to specific administration instructions

Approved petition does not guarantee future ANDA approval

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