

Decision Framework for Section 505(b)(2) Drug Products

OVERVIEW

1. Information gathering (pg. 2)

- Applicable billing and payment codes
- FDA-approved drug product labeling
- United States Pharmacopeia – National Formulary (USP-NF) nomenclature

2. Drug Product Evaluation (pg. 3)

- Match
- Non-Match

3. Verification Step – Pharmacokinetic and clinical studies in labeling (pg. 4)

- Match
- Non-match

Determination (pg. 5)

Assign to existing
multiple source code

Assign to single source
code

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Information Gathering

Following marketing and sales of a section 505(b)(2) drug product that is payable under Medicare Part B, the information below is gathered by the Centers for Medicare and Medicaid Services (CMS) for the purpose of applying the framework.

Billing and Payment Codes

Determine whether there are multiple source drug codes (e.g., Healthcare Common Procedure Coding System (HCPCS) codes) that may contain drug products that correspond to the section 505(b)(2) drug product. For example, if the descriptor of the multiple source drug code contains the same drug name or active ingredient as the section 505(b)(2) drug product.

If a multiple source drug code is not identified, the framework assessment is not necessary and the section 505(b)(2) drug product should be assigned to a single source drug code.

If more than one multiple source drug code is identified, the framework assessment should be applied separately for each existing code identified.

Labeling

Obtain for the section 505(b)(2) drug product and drug product(s) assigned to the multiple source drug code

Most recent FDA-approved labeling

Drug Product Name

Obtain for the section 505(b)(2) drug product and drug product(s) assigned to the multiple source drug code

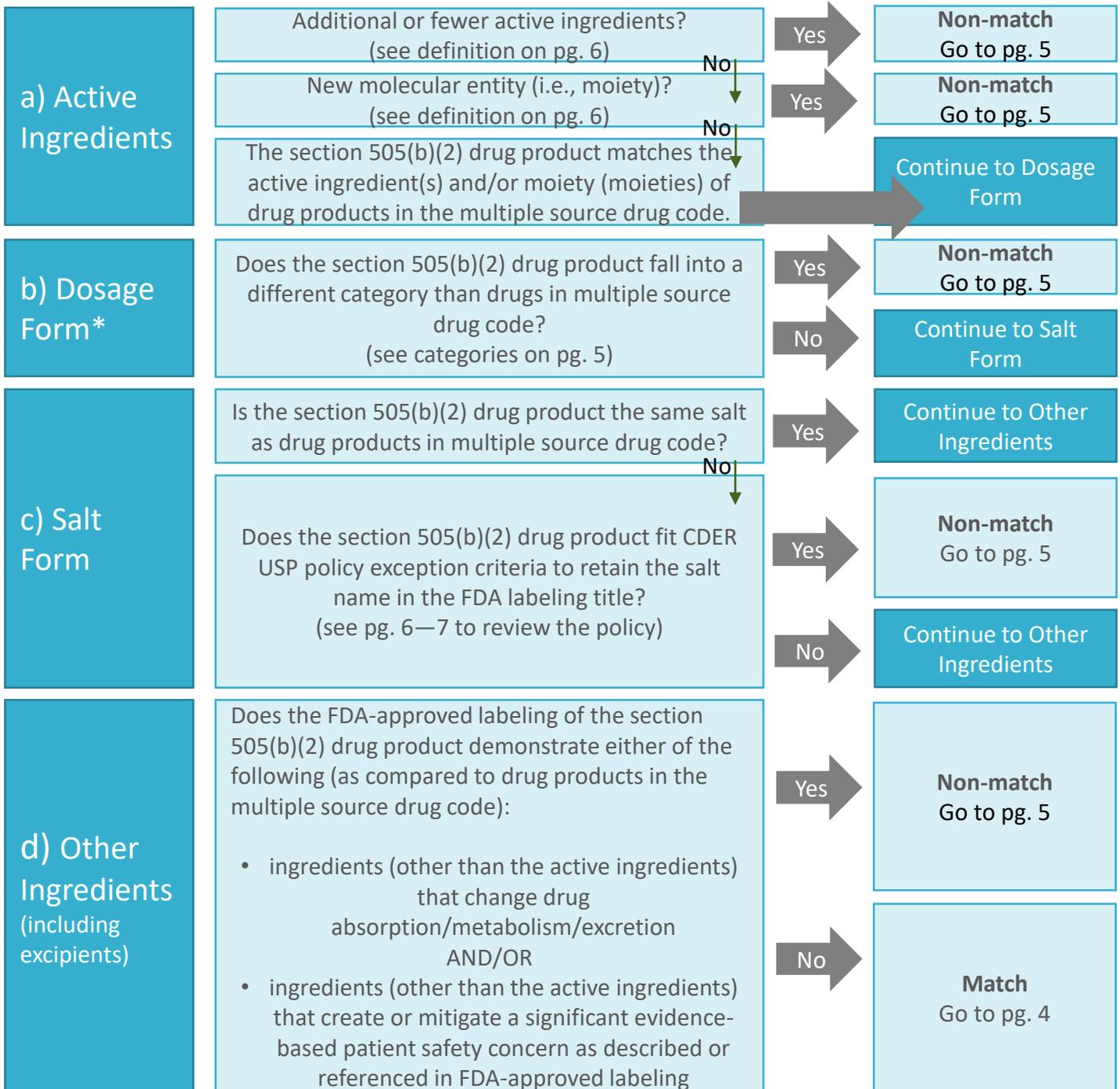
USP-NF nomenclature
[DRUG-usually USAN] [ROUTE OF ADMINISTRATION-where applicable]
[DOSAGE FORM-where applicable]

FDA nomenclature as stated in the labeling title

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Drug Product Evaluation



* Complete step (b), dosage form, only if it is part of the drug product name information gathered from the USP-NF or the FDA-approved labeling. If the dosage form is not included, continue to step (c), Salt Form

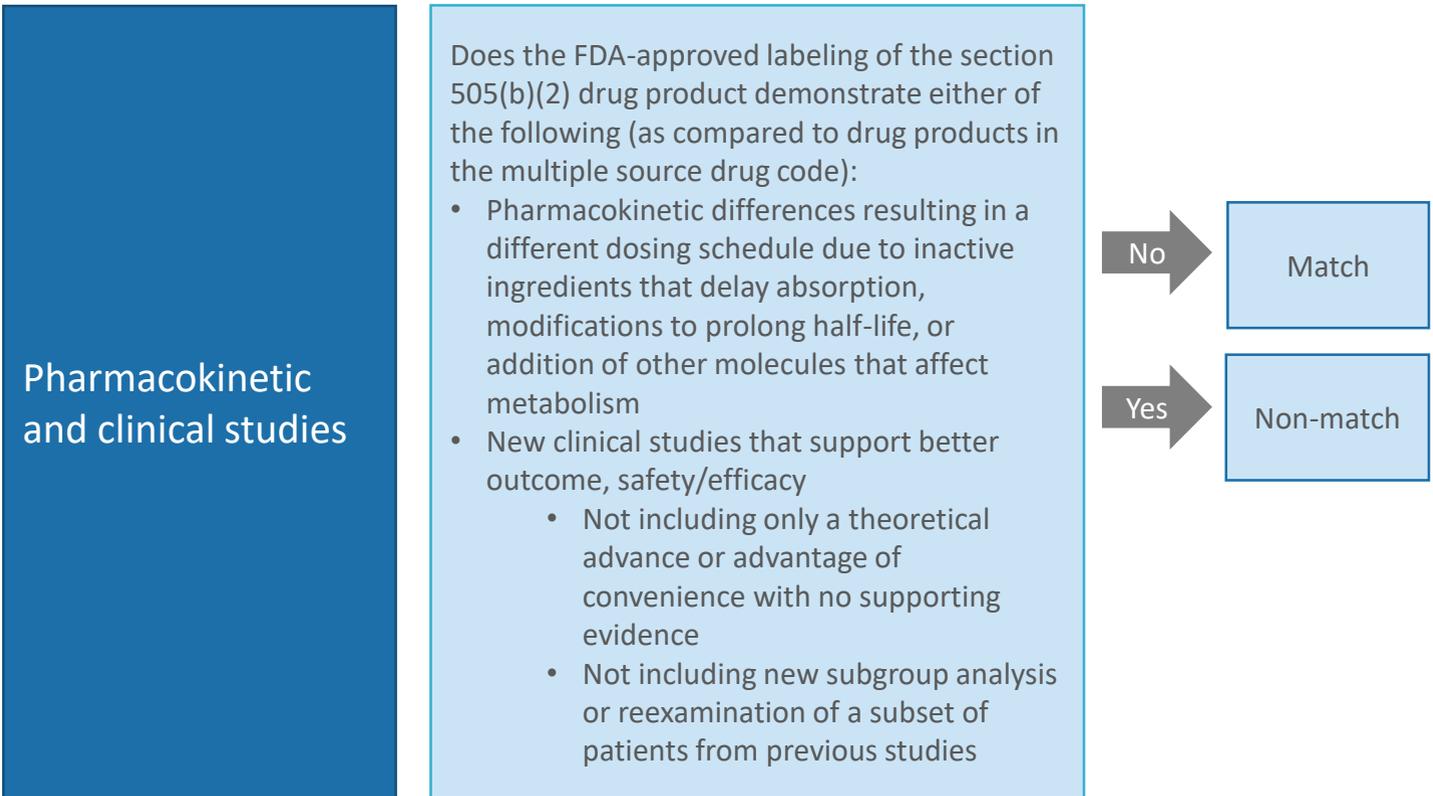
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Verification Step

Pharmacokinetic and Clinical Studies in FDA-approved Labeling

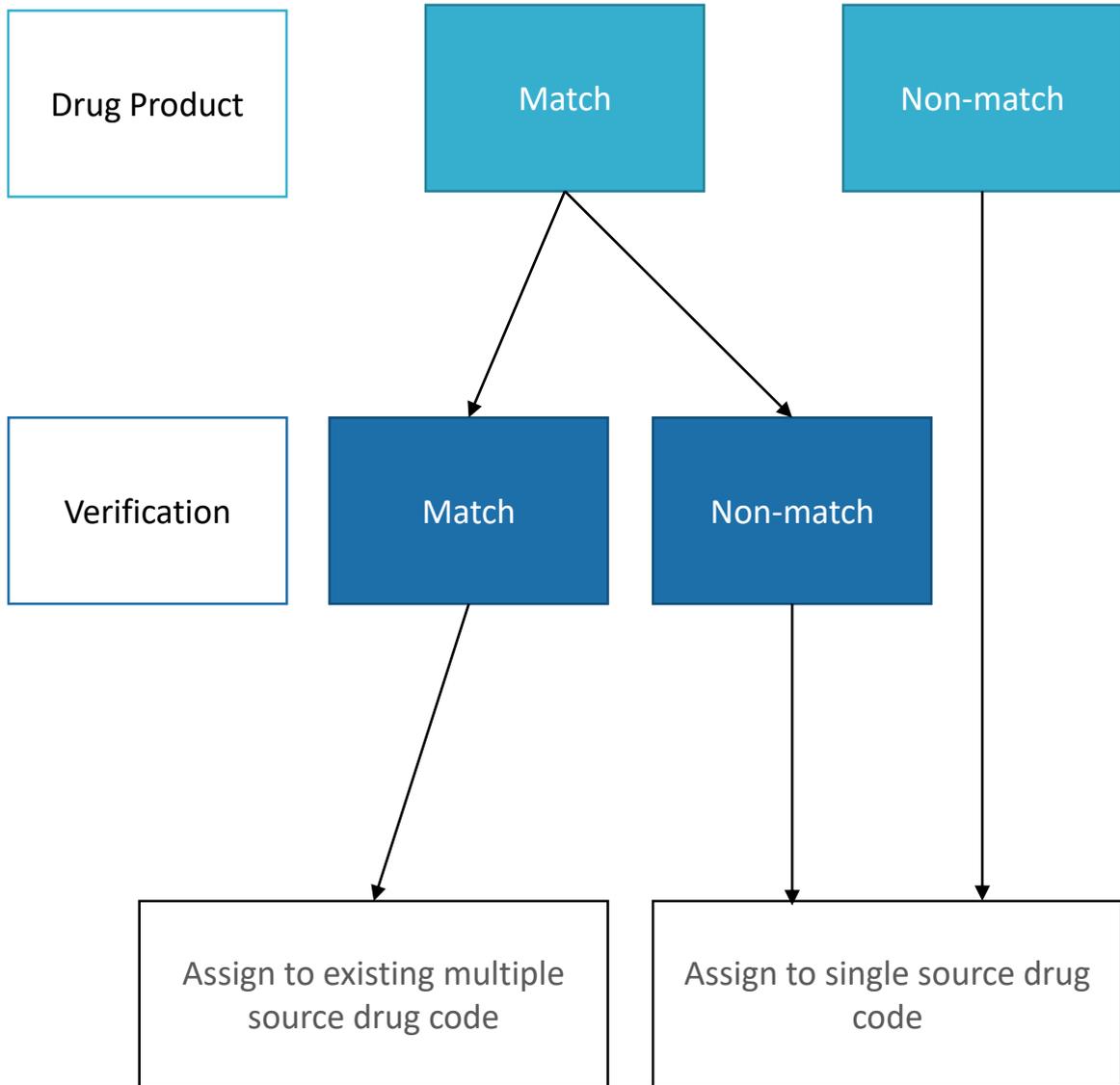
The verification step is completed for any section 505(b)(2) drug product that was determined to be a “Match” in the previous step.



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Decision Framework Determination



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Drug Product Evaluation

Additional background information needed for the Drug Product Evaluation.

FDA definitions¹ (use on pg. 3, part (a)):

- **Active ingredient** is any component that is 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 body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.
- **Active moiety** is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

Categories for dosage form assessment (use on pg. 3, part (b)):

- Injectable (for example, IV, IM, subcutaneous, intradermal, etc...²)
- Implant
- Oral, sublingual, buccal
- Ophthalmic
- Other topical

USP and FDA conventions and salt policy³ (use on pg. 3 part (c)):

The USP Salt Policy is a naming and labeling policy applicable to drug products that contain an active ingredient that is a salt. The policy stipulates that USP will use the name of the active moiety, instead of the name of the salt, for such a drug product when creating a drug product monograph title. The USP Salt Policy also states that USP will base the strength of the product on the active moiety. The policy allows for exceptions under specified circumstances. See specific exclusions below.

1. The name of the salt could be retained if any of the following safety or historical conditions are met:
 - a) The active ingredient is a relatively simple salt and administration of the entire salt is therapeutically important. Examples include: lithium carbonate; iron sulfate, and other oral and intravenous iron salts; calcium gluconate and other calcium salts; potassium chloride; magnesium sulfate; sodium or potassium phosphate; and sodium citrate.

1. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=314.3>

2. We note that this is not an exhaustive list of dosage forms. Appendix C of the "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations," available at <https://www.fda.gov/media/71523/download>

3. <https://www.fda.gov/media/87247/download>

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Drug Product Evaluation

USP and FDA conventions and salt policy cont.:

- b) Scientific evidence demonstrates the salt form affects the absorption, distribution, metabolism, and/or excretion (ADME) of the drug in a manner that influences the clinician's product selection.
 - c) Clinically significant amounts of cations (e.g., sodium, potassium, magnesium or calcium) accompany the active moiety of a drug product. Clinical significance may be related to the recommended maximum daily amount of an electrolyte intake in special patient populations. Examples include: recommended daily intake of sodium in patients with congestive heart failure or recommended daily intake of potassium in patients with chronic kidney disease.
 - d) There is a significant evidence-based safety concern that the counter-ion part of the salt could cause acid-base disturbances, hepatic, renal or other organ damage, or hypersensitivity reactions.
2. The name of the salt could be retained if any of the following safety or historical conditions are met:
- a) The name of the salt is necessary to maintain consistency with other dosage forms of the same active ingredient (salt). For example, if a tablet dosage form that was approved before May 1, 2013 included the salt in its established name and the drug product's strength is based on the salt form, the naming convention would not change for a new capsule dosage form with the same active ingredient (salt) that is approved after the effective date.
 - b) The FDA identifies that the USP Salt Policy should not be applied because there are relevant, documented safety reasons (e.g., documented medication errors related to name or strength) in a closely related product.
 - c) If the FDA names a drug product according to the USP Salt Policy (e.g., the name and strength of the product are based on the active moiety) and, postapproval, there are safety concerns, we will consider whether a retrospective name change is appropriate. CDER and USP have agreed to coordinate any retrospective name changes.

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