Guidance for Implementation and Exceptions:
The Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations in General Chapter <1121> Nomenclature

A. Overview and Background

USP Nomenclature Guidelines state the following policy regarding drugs products containing salts:

> "The titles of USP monographs for drug products and compounded preparations formulated with a salt of an acid or base generally use the name of the active moiety. The strength of the product or preparation is also expressed in terms of the active moiety.
>
> An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be a salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule."

This Policy is followed by USP in naming drug products and compounded preparations that are newly recognized in the USP.[1]

USP does not anticipate changing existing monograph titles unless necessary for safety. USP and FDA CDER have agreed to coordinate regarding any necessary retrospective name changes.[2] This Guidance is provided to help provide consistency in considerations for implementation or exceptions to the policy.

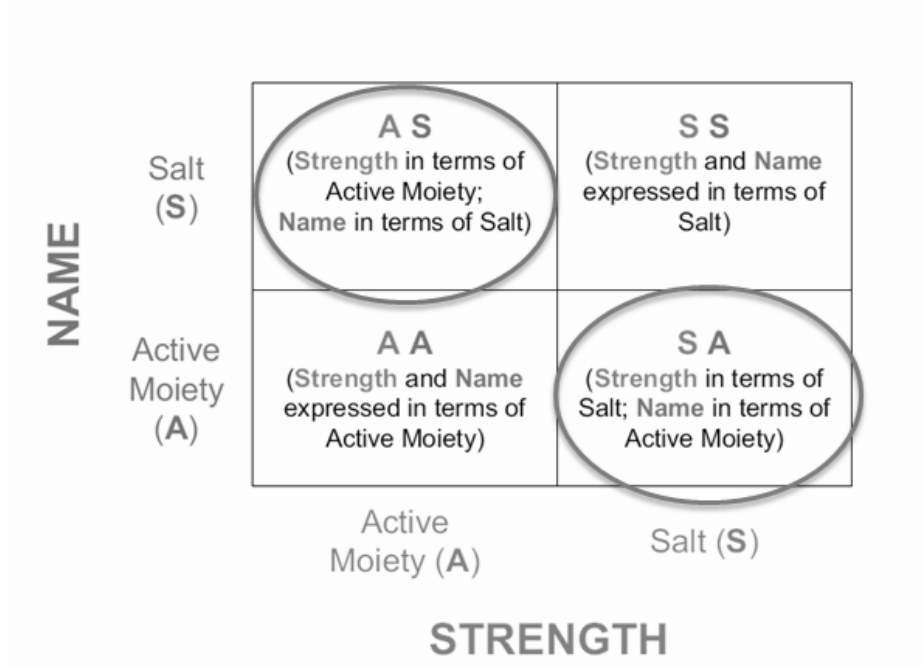
When naming monograph drug products and compounded products, the practical downstream impact of a selected drug product title must be considered. Drug names can influence ease of understanding, and the potential of confusion in product selection or medication errors. Healthcare information needs to be as clear and consistent as possible for healthcare professionals and patients to make decisions when prescribing, dispensing, administering, or selecting drug products.

B. Historical Titles

Some new monographs are developed for drug products that have been on the market for many years. Such monographs will not easily incorporate the requirement of General Chapter *<1121> Nomenclature* to use active moiety in the name and strength definition. These products will need to be considered under an exception on a case-by-case basis.

C. Considerations for Salt Nomenclature

Implementation of the policy applies to a mismatch of Name and Strength for two combinations out of four possible options: A S and S A as outlined by the circles below.



D. <u>Review Scheme for Proposed Titles</u>

1. Similar products

Identify products containing:

a. The same drug substance, but different dosage forms. Commonly considered "family effect."
b. The same active moiety, but different chemical forms (salt, base) that are also marketed.
c. The same drug substance in combination products

2. Similar situations

Similar situations can identify significant issues that have impacted previous title decisions and can include any of the following:

a. Historical context
b. Past compendial/*PF*/NL decisions
c. Drug family implications
d. Error potential

Similar situations can be presented and filed in a way that captures key features. Such documentation can provide further insight about previous nomenclature decisions made under similar circumstances.

3. Impact on healthcare professionals and patients

Elements to be considered in the assessment:

a. Historical Titles
   i. Length of time on the market
   ii. Number of products in the same product family
   iii. USP Monographs: Length of time and number of monographs

b. Different routes of administration and/or different dosage forms
   Relevance to title choice based on precedent for different product types (e.g., capsules, tablets, ophthalmic solutions)

c. Potential for medication errors or confusion in product selection
   Official title selection criteria should consider risk of medication errors or confusion in product selection as an important component of the review process, and recommendations should attempt to avoid problem titles.

d. Scientific evidence demonstrates that the salt form affects the pharmacokinetic properties of the drug in a manner that can influence product selection.[2]

e. Clinically significant amounts of cations (e.g., sodium, potassium, magnesium or calcium) that accompany the active moiety of a drug product.[2]
   i. In cases in which the use of the specific salt form of the active moiety in the title provides vital information from a clinical perspective, an exception to this policy may be considered. In such cases, when the monograph title contains the specific salt form of the active moiety, the strength of the product or preparation is also expressed in terms of the specific salt form.
   Examples: Penicillin G Potassium for Injection
   Penicillin G Sodium for Injection

f. Other significant evidence-based safety concerns.[2]

4. Simple Salts

The significance of a simple salt may be important for administration. The entire salt would be deemed therapeutically important for healthcare providers.[2]

Examples: Calcium Gluconate
Sodium Lactate

E. <u>Summary of Considerations included in Ballot for each proposed monograph title</u>

The reasons noted above are neither exhaustive nor limiting and other concepts may need to be considered. A comment should be included as part of each ballot containing a proposed monograph title for a salt-containing active ingredient. The comment will include an appropriate summary of issues relevant to that specific drug and title as the basis for nomenclature recommendation. Such comments could guide staff preparing ballots, serve as an educational tool for nomenclature

committee members considering ballots, and provide a useful archive of how each decision was reached.

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[1] USP. *Nomenclature Guidelines*. Rockville, MD: USP; February 1, 2018. https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/nom_guidelines.pdf

[2] US Food and Drug Administration. Guidance for Industry. Naming of Drug Products Containing Salt Drug Substances. Silver Spring, MD: US Food and Drug Administration, Center for Drug Evaluation and Research; June 2015. https://www.fda.gov/media/87247/download. Accessed April 29, 2019.

SUMMARY OF CHANGES FOR THIS REVISION:

SUMMARY OF CHANGES	RATIONALE FOR CHANGE
G01.19-00	
New Document	NA