Commentary

April 2024 Accelerated Revisions

April 26, 2024

In accordance with USP's *Rules and Procedures of the Council of Experts ("Rules*"), and except as provided in Section 9.02 *Accelerated Revision Processes*, USP publishes proposed revisions to the *United States Pharmacopeia and the National Formulary* (*USP–NF*) for public review and comment in the *Pharmacopeial Forum (PF),* USP's free bimonthly journal for public notice and comment. After comments are considered and incorporated as the Expert Committee (EC) deems appropriate, the proposal may advance to official status or be re-published in *PF* for further notice and comment, in accordance with the Rules. In cases when proposals advance to official status*,* a summary of comments received and the appropriate Expert Committee's responses, as well as Expert Committee-initiated changes, are published in the Proposal Status/Commentary section of USPNF.com at the time the official revision is published.

The *Commentary* is not part of the official text and is not intended to be enforceable by regulatory authorities. Rather, it explains the basis of Expert Committees' responses to public comments on proposed revisions. If there is a difference or conflict between the contents of the *Commentary* and the official text, the official text prevails.

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No comments were received for the following when they were proposed in Pharmacopeial Forum:
Zinc Sulfate

Comments were received for the following when they were proposed in Pharmacopeial Forum:

Monographs
Acyclovir
Zinc Acetate
Zinc Chloride

Monographs

Monograph/Section(s): Acyclovir/Organic Impurities
Expert Committee: Small Molecules 1
No. of Commenters: 3
Comment Summary #1: The commenter indicated that the 7,9' Diguanyl and 9,9'-Diguanyl analogs are coeluting even after adjustments as per GC <621> and use of different columns.
Response: Comment not incorporated. The supporting validation data showed baseline resolution for the 7,9' Diguanyl and 9,9'-Diguanyl analogs and was confirmed by an example chromatogram.

Comment Summary #2: The commenter indicated that their specificity data showed an RRT of 1.48 for the Diacetyl guanine. The commenter confirmed that they did not observe the degradation of Diacetyl guanine to *N*-Acetylguanine during sample analysis.
Response: Comment not incorporated. The supporting validation and characterization data confirmed the updated RRTs for *N*-Acetylguanine and Diacetyl guanine are 1.48 and 2.36, respectively.

Comment Summary #3: The commenter indicated that they observed the degradation of Diacetyl guanine to *N*-Acetylguanine during sample analysis. Therefore, they were not able to perform validation of the method.
Response: No action taken. The supporting validation data reported the same degradation pathway. However, the method was successfully validated, and the Expert Committee supported the proposal as written with the limits for Diacetyl guanine be maintained at NMT 0.1% and N-Acetylguanine is as an unspecified impurity.

Comment summary #4: The commenter recommended removing the reporting threshold in the test for Organic Impurities as it will vary based on product-specific factors.
Response: Comment not incorporated. A new USP general chapter, ⟨477⟩ *User-Determined Reporting Thresholds* supports a flexible reporting threshold to accommodate product-specific factors. The Expert Committee will consider incorporating this new approach in future revisions, as applicable.

Monograph/Sections: Zinc Acetate /Multiple sections
Expert Committee(s): Small Molecules 2
No. of Commenters: 2

Comment summary #1: The commenter recommended USP to tighten the acceptance criteria for 'Arsenic' and 'Lead' to be in line with ICH Q3D guidelines.
Response: The comment is out of the scope of this revision. The Expert Committee will consider future revisions to the monograph upon the receipt of supporting data.
Comment summary #2: The commenter recommended USP to include tests for 'Aluminum' and 'Iron' with acceptance criteria consistent with what have been approved by the FDA and recommend USP to contact the FDA approved applicants to obtain the relevant information.
Response: Comment partially incorporated. USP reached out to a manufacturer and received no response. The Expert Committee will consider future revisions to the monograph upon the receipt of supporting data.

Monograph/Sections: Zinc Chloride /Assay

Expert Committee(s): Small Molecules 3
No. of Commenters: 3

Comment summary #1: The commenter recommended revising the acceptance criteria for *Assay* to be what was in the official monograph prior to the publication of *PF* 46(6).
Response: Comment not incorporated. The comment is out of the scope for this revision. The Expert Committee will consider future revisions to the monograph.
Comment summary #2: The commenter recommended revising the ammonia test in line with the European Pharmacopoeia (EP) monograph.
Response: Comment not incorporated. The comment is out of the scope for this revision. The Expert Committee will consider future revisions to the monograph upon the receipt of supporting data.

Comment summary #3: The commenter recommended revising the USP Monograph for Zinc Chloride to the previously official assay titration method.
Response: Comment not incorporated. The comment is out of the scope for this revision. The Expert Committee will consider future revisions to the monograph.