Commentary
USPNF 2026 ISSUE 3

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In accordance with USP's *Rules and Procedures of the 2025-2030 Council of Experts* (*CoE Rules*), and except as provided in Section 10.02 *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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Comments were received for the following when they were proposed in Pharmacopeial Forum:

General Chapters
<621> CHROMATOGRAPHY
Colistimethate Sodium

General Chapter

General Chapter:	<621> CHROMATOGRAPHY
Expert Committee:	Chemical Analysis
No. of Commenters:	12

System Sensitivity
Comment Summary #1: The commenter requested information on the solution that the signal-to-noise (S/N) ratio should be checked. The commenter also inquired whether the system sensitivity requirement does not have to be checked if there is no standard deviation (STD) or system suitability test (SST). In addition, the commenter questioned whether "System Sensitivity" only applied to quantitation tests for impurities and asked for more guidance.
Response: Comment not incorporated. The chapter clearly defines where the test is applied and how it is applied. The proposed text states "In impurity tests, when the procedure in a monograph prescribes the use of a reporting threshold."

Comment Summary #2: The commenter indicated that in monographs the reporting threshold is often defined as 0.05%. Referencing the General Notices 7.20 Rounding Rules, the commenter asked about the preparation accuracy of the reference solution used for assessing the reporting threshold.
Response: Comment not incorporated. The comment is outside the scope of this chapter. Such questions are addressed in General Notices and Chapter <477> User Determined Reporting Thresholds.

Comment Summary #3: Two commenters suggested revisions to the determination of signal-to-noise ratio entry. The first commenter suggested adding "and blank solution (reference solution lacking active substance)" to the procedure for determination of signal-to-noise ratio. The commenter also recommended revising the acceptance criteria entry “(corresponding to a signal-to-noise ratio of 10)" to state "(corresponding to a signal-to-noise ratio of 10:1)". The second commenter stated that the system sensitivity requirement to be met is unclear and recommended revising it to state "the reporting threshold solution should have a signal-to-noise ratio greater than 10."
Response: Comments partially incorporated. For the definition of reporting threshold and measurement procedure the text was revised to state "the signal-to-noise ratio of the analyte (official substance) peak from the chromatogram of a solution at the concentration corresponding to the reporting threshold is used to define the system sensitivity."
The text concerning the acceptance criteria was revised to state "The system sensitivity requirement is met if the signal-to-noise ratio is not lower than (NLT) 10.”

Peak Symmetry

Comment Summary #4: The commenter suggested to further clarify whether quantification tests include impurity testing, noting that their understanding is that the requirement applies to quantitative tests.
Response: Comment not incorporated. The chapter text clearly defines where it is applied, "in the Organic Impurities test, Related Substances test, or the Assay."

Comment Summary #5: The commenter suggested also applying the waiver of thepeak symmetry requirement in the Organic Impurities and Related Substances tests to Assay tests.
Response: Comment not incorporated. The waiver cannot be done for the assay because the risk of error is high since some impurities may be hidden in the tailing of a large main peak.

Comment Summary #6: The commenter recommended clarifying that percentage relative standard deviation in the System Suitability test is measured for the peak response by replacing "determination of the percentage relative standard deviation" with "determination of the percentage relative standard deviation of peak response."
Response: Comment incorporated. The text was revised to state "determination of the percentage relative standard deviation of peak response is prescribed as part of the System Suitability test."

Comment Summary #7: The commenter recommended revising the first sentence of the Peak Symmetry subsection to replace "Peak Symmetry: Unless otherwise stated, in the Organic Impurities test, Related Substances test, or the Assay," with "Peak Symmetry: Unless otherwise stated, in the Monograph Organic Impurities test, Related Substances test, or the Assay".
Response: Comment not incorporated. The requirement also applies to tests in other General Chapters.

Comment Summary #8: The commenter suggesting revising the text to narrow the application of the symmetry factor requirements to only apply to Chromatographic Purity test, Organic Impurities test, Related Substances test and Assay test by Liquid chromatography.
Response: Comment not incorporated. The text is clear that the symmetry factor requirements are applicable to all chromatographic procedures.

Reporting Threshold

Comment Summary #9: Three commenters recommended against the proposed deletion of the sentence "In such tests the reporting threshold, i.e., the limit above which a peak is reported, is defined generally 0.05%." The first commenter stated that there is a need to incorporate the reporting threshold for specifically Assay and single peak analysis. The second commenter noted that in their opinion a general information/procedure for setting a reporting threshold is useful, especially if there is no reporting threshold given in the monograph. The third commenter stated that this same limit statement is present within the PhEur 2.2.46, Chromatographic separation techniques, and the JP 2.00, Chromatography. The third commenter said that if this statement is being removed in order to focus on limits provided within individual monographs, they advocate for retaining some guidance for those monographs that do not include such a limit.
Response: Comments not incorporated. The first recommendation is outside the scope of this chapter. Regarding the rationale that the two other comments presented, the compendia (USP-NF) addresses the reporting threshold in General Chapter <477> User Determined reporting Thresholds.

DEFINITIONS
Comment Summary #10: The commenter suggested revising the signal-to-noise definition to state "The signal-to-noise ratio is based on a baseline of 20 times the peak width at half height but if this is not obtainable, a baseline of at least 5 times the width at half-height is permitted."
Response: Comment not incorporated. The official text is clear. It states "at least 5 times," and the users can use a larger range than 5 times if they choose to.

Comment Summary #11: The commenter recommended adding a title to Figure 7 under the Definitions Section to state "Figure 7: Chromatogram of the blank solution."
Response: Comment incorporated. “Chromatogram of a blank solution” was added as caption for Figure 7.

System Repeatability
Comment Summary #12: The commenter recommended adding the % character after the 2.0 requirement in the “System Repeatability” subsection.
Response: Comment incorporated.

Definition
Comment Summary #13: The commenter recommended revising the dwell volume definition to state, “The dwell volume (also known as gradient delay volume) is the volume that the mobile phase mixture must travel to be injected into the column.”
Response: Comment not incorporated. The recommendation is outside the scope of this revision. Moreover, this is a harmonized text. The Expert Committee will consider the recommendation in a future revision as part of the harmonization process.

Comment Summary #14: The commenter recommended that the structure of this General Chapter be split up, in order to make it easier to update technique-specific general chapters that include essential Analytical Instrument Qualification requirements to align with USP <1058>. The commenter noted that the scale of this change means providing specific comments on this integrated chapter <621> is difficult.
Response: Comment not incorporated. The commenter's comments are outside the scope of the revision. The chapter is a harmonized chapter. The Expert Committee will consider the recommendation in the future and share with other pharmacopeias of Pharmacopeia Discussion Group (PDG).

Monograph

Monograph: Colistimethate Sodium
Expert Committee(s): Small Molecules 1
No. of Commenters: 1

Comment Summary #1: The commenter indicated that the starting material, colistin sulfate, would need to meet the requirement of 50.0%–75.0% colistin A and 5.0%–20.0% colistin B to comply with the acceptance criteria in the composition test. Therefore, the commenter requested not to implement the composition test.

Response: Comment not incorporated. Colistimethate sodium for parenteral use in humans should meet the requirements of the composition test. Colistin sulfate in other compositions is used for topical human use or for veterinary use.