***Commentary***

***Pharmacopeial Form 45(3)***

September 27, 2019

In accordance with USP's Rules and Procedures of the Council of Experts ("Rules"), and except as provided in Section 7.02 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 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 without re-publication in *PF,* a summary of comments received and the appropriate Expert Committee's responses are published in the Revisions and Commentary section of USP.org 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 between the contents of the *Commentary* and the official text, the official text prevails. In case of a dispute or question of interpretation, the language of the official text, alone and independent of the *Commentary*, shall prevail.

For further information, contact:
USP Executive Secretariat
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA

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

***General Chapters***
<467> Residual Solvents

***Monographs***
Atropine Sulfate Ophthalmic Solution (deferred from previous *PF*)

---

**General Chapter:** <467> *Residual Solvents*
**Expert Committee:** General Chapters—Chemical Analysis
**No. of Commenters:** 10

***1. General***
**Comment Summary #1:** Commenters noted that ICH is in the process of changing the PDE for Ethyleneglycol back to 6.2 mg/day, therefore they suggest USP does the same.
**Response:** Comment incorporated. The PDE for Ethyleneglycol in <467> is not changed and remains at 6.2 mg/day (see Updated Notice of Intent to Revise: <467> Residual Solvents ).
**Comment Summary #2:** Commenter questioned the proposed implementation timeline for reclassification of methylisobutylketone (MIBK) from a Class 3 Residual Solvent to a Class 2 Residual Solvent and the introduction of trimethylamine (TEA) as a new Class 3 Residual Solvent. They requested a delayed implementation to allow enough time for the respective companies to perform the activities needed for the change.
**Response:** Comments incorporated. USP decided to delay the implementation time for the reclassification of MIBK from a Class 3 Residual Solvent and introduction of TEA as a Class 3 Residual Solvent from December 1, 2019 to December 1, 2020.

***2. Section 8.1 Chromatographic Systems - Figure 4***
**Comment Summary #3:** Commenters noted that the revised system suitability resolution criteria for Procedure B had not been incorporated in Figure 4.
**Response:** Comment incorporated. The text for the resolution in the Figure 4 bottom left corner's last box is changed from: Rs: ACN-DCE BK is NLT 1.0 to Rs: DCE-MI is NLT 1.0.

---

**Monograph/Sections:** Atropine Sulfate Ophthalmic Solution/Multiple sections
**Expert Committee:** Chemical Medicines Monographs 4
**No. of Commenters:** 2
**Comment #1:** The commenters requested revising the chromatographic procedure in the test for *Organic Impurities* to be more specific for other potential impurities.
**EC Response:** Comment not incorporated. The Expert Committee will consider future revisions to the monograph upon receipt of all of the necessary supporting information.
**Comment #2:** The commenter requested revising the test for *Organic Impurities* so that the *Resolution* requirement between atropic acid and atropine could be met.
**EC Response:** Comment incorporated as follows. The *Resolution* requirement between atropic acid and atropine is revised from NLT 3.0 to NLT 1.5. The Expert Committee will consider future revisions to the monograph upon receipt of all of the necessary supporting information.

**EC-Initiated Change #1:** *Identification B*, the wet chemistry test for the presence of sulfate has been removed as the counterion could be present due to excipients.
**EC-Initiated Change #2:** *Identification C* has been renamed *Identification B* and all references to *Identification C* are updated to *Identification B*.
**EC-Initiated Change #3:** The *Sensitivity solution*, *Signal-to-noise ratio* requirement, and reporting threshold have been removed from the test for *Organic Impurities* as the proposed reporting threshold of 0.10% is not necessary (the limit for any individual unspecified degradation product is NMT 1.0%). The Expert Committee will consider future revisions to the monograph upon the receipt of a validated procedure which is more sensitive and all the necessary supporting information.
**EC-Initiated Change #4:** Throughout the monograph, the molecular weights for atropine sulfate monohydrate and anhydrous are updated from 694.83 and 676.83 to 694.84 and 676.82, respectively.