



**Monograph/Section:** Phenoxybenzamine Hydrochloride/Organic impurities

**Expert Committee:** Small Molecules 2

**No. of Commenters:** 1

**Comment Summary #1:** The commenter commented: Phenoxybenzamine aziridinium can be formed both in-situ of chromatographic analysis and during the manufacturing process or storage. Phenoxybenzamine aziridinium present in this drug substance prior to chromatographic analysis could be overlooked when it is excluded from the acceptance criteria of any unspecified impurity and Total impurities. Phenoxybenzamine aziridinium can convert to Phenoxybenzamine alcohol, resulting in the overestimation of Phenoxybenzamine alcohol. If Phenoxybenzamine aziridinium is present in significant amounts, it may affect the Assay results.

The commenter recommended developing a suitable test to analyze the content of Phenoxybenzamine aziridinium.

**Response:** Comment not incorporated. Phenoxybenzamine aziridinium can convert to Phenoxybenzamine alcohol which is controlled as a specified impurity in the monograph proposal. However, supporting data is not available for overestimation of Phenoxybenzamine alcohol due to the presence of Phenoxybenzamine aziridinium.

Formation of Phenoxybenzamine aziridinium, in situ of the chromatographic analysis, would be at similar rates for the Standard solution and the Sample solution in the Assay. There is no data indicating the Assay result being significantly affected by Phenoxybenzamine aziridinium formation.

The Expert Committee will consider future revisions to the monograph upon receipt of additional supporting data.

**Comment Summary #2:** The commenter recommended removing the “reporting threshold” as it will vary based on product-specific factors.

**Response:** Comment not incorporated. USP is considering the issue of removing reporting thresholds from certain monographs. A proposal for a new general chapter, <477> *User-Determined Reporting Thresholds*, was published in *PF 48(5)* for public comment. The responsible Expert Committee will review the comments and determine the next steps for the chapter.

**Comment Summary #3:** The commenter recommended removing the alternate name, Phenoxybenzamine tertiary amine, for Phenoxybenzamine alcohol, because it can be misleading considering both Phenoxybenzamine alcohol and the drug substance are phenoxybenzamine tertiary amines.

**Response:** Comment incorporated.