General Chapter Prospectus: <1469> Nitrosamine Impurities

Posting Date: 24–Apr–2020
Expert Committee: General Chapters—Chemical Analysis
Input Deadline: 22–May–2020
Proposed New Title: <1469> Nitrosamine Impurities.

Suggested audience: Suppliers and manufactures of drug substance, drug products, excipients, contract manufacturing organizations, drug testing organizatic

Estimated proposal PF: *Pharmacopeial Forum* 46(5) [Sep.–Oct. 2020]

Background and objective(s): USP intends to develop a new informational general chapter to align with current scientific and regulatory approaches to prov impurities in drug substances and drug products.

Description of scope and application: To provide a risk-based approach for the control of nitrosamine impurities in order to reduce or eliminate their preser analytical procedures used in the Identification and quantification of nitrosamine impurities.

Preliminary outline: The following represents the sections for the proposed General Chapter

- INTRODUCTION
- SOURCES OF NITROSAMINES-The sources by which the nitrosamines could be introduced in pharmaceutical products include, but are not limited t impurities in raw materials, recycled solvents, reagents or catalysts; c) synthetic pathways; d) as impurities in some packaging systems; etc.
- NITROSAMINE RISK ASSESSMENT- DEVELOPMENT OF A CONTROL STRATEGY- A flow chart for a control strategy which also incorporate processes in the production of drug substance and/or drug products for the likelihood of nitrosamine presence.
- LIMITS OF NITROSAMINES-The section provides information on how to derive drug product concentration limits based on the acceptable daily intal
- TEST PERFORMANCE CHARACTERISTICS OF NITROSAMINE PROCEDURES – This section provides recommended acceptance criteria for an nitrosamines
- IDENTIFICATION, CONTROL, AND QUANTIFICATION OF NITROSAMINES-Several analytical procedures are included in this section with the official articles for which they have been validated or verified. The section includes considerations for sample preparations based on the experience of U

Anticipated implementation timing: To be determined based on stakeholder feedback.

Additional Information: USP has developed a comprehensive portfolio of USP Reference Standards for nitrosamine impurities including, N-Nitrosodimeth (NDIPA), N-Nitrosodibutylamine (NDBA), N-Nitrosoethylisopropylamine (NEIPA), and N-Nitrosomethylaminobutyric Acid (NMBA). The new reference

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