



Frequently Asked Questions Regarding the Implementation of USP General Chapters <232> Elemental Impurities—Limits and <233> Elemental Impurities—Procedures

Version 2: June 7, 2013

1. Are General Chapters <232> Elemental Impurities—Limits and <233> Elemental Impurities—Methods currently official? Are the new general chapters applicable to any monographs?

Both General Chapters <232> and <233> became official February 1, 2013, but are not applicable to any monographs at this time.

2. How does USP plan to apply General Chapters <232> and <233> to monographs? Do they apply to all monographs or just to drug products?

USP plans to apply General Chapters <232> and <233> to monographs via a proposed provision (5.60.30) in General Notices. General Chapters <232> and <233> will apply only to drug product monographs currently in the *USP-NF*.

3. USP has deferred the proposed General Notices provision 5.60.30 Elemental Impurities. What is a “deferral” and what are the possible outcomes?

USP’s standards-setting process requires that a standard be balloted by the responsible Expert Committee before it is published and becomes official. Under certain circumstances, e.g., when public comments indicate the need for a standard or part of a standard to be reconsidered, the Expert Committee may choose to defer the balloting of the text in question to allow time for additional review. Following a deferral, the standard may be balloted at a future date in its original or slightly modified form. Typically if the Expert Committee decides to significantly modify the original proposal, it would be repropose for public comment, or canceled altogether.

4. Why has USP deferred the proposed General Notices provision 5.60.30 Elemental Impurities?

USP believes that manufacturers need a single set of tests with limits (acceptance criteria) for drug products affected by the improved testing of elemental impurities described in <232> and <233>. USP expects the ICH Q3D EWG to conclude a Step 2 document soon, which will allow USP to align the elements and limits (acceptance criteria) in the ICH document with those in General Chapters <232> and <233>. In addition, USP believes a reasonable timeframe for implementation needs consideration based on comments received on the General Notices provision 5.60.30 as it appeared in PF 39(1).

5. How long will the General Notices provision be deferred? How will USP assess the implementation issues?

USP has not yet established a new implementation date for General Notices 5.60.30. USP believes time is needed to adjust General Chapters <232> and <233> and for drug product manufacturers to implement the new requirements. The USP Council of Experts will consider the recommendations from an Advisory Group that will consist of scientific experts from industry and the Food and Drug Administration (FDA) who will assess the implementation issues. Based on these recommendations, the Council of Experts,

balancing manufacturer needs with public health impact, will decide the implementation timing.

6. How will the Advisory Group be formed? Who will be its members?

In accordance with the Bylaws of the USP Convention, “The EVP-CEO may appoint advisory bodies to advance the work of the Council of Experts and the Convention and provide advice to staff on policy matters.” In this case, Dr. Roger Williams has appointed an Advisory Group on the Implementation of General Chapters <232> and <233>. The members comprise:

- Representatives of key trade organizations that submitted comments to USP on the implementation of the General Chapters
- Three representatives of FDA
- The rapporteurs of the ICH Q3D Expert Working Group
- The chair of USP’s Toxicology Expert Committee

See the announcement about the Advisory Group on the [Elemental Impurities Key Issues Page](#).

7. How will USP coordinate with the ICH Expert Working Group (EWG) Q3D on Elemental Impurities? How will the General Chapters be updated to align with ICH limits?

USP is participating in the ICH Q3D process as an observer and looks forward to a Step 2 document in June.

8. Does USP plan to make revisions to General Chapters <232> and <233>?

Adjustments are expected through the decision-making process of the Council of Experts. The adjustments will be proposed by the Elemental Impurities Expert Panel to the Chemical Analysis Expert Committee. USP will post further information about future revisions to <232> and <233> in the Key Issues: [Elemental Impurities](#) area of its website.

9. Will General Chapter <231> be omitted once General Chapters <232> and <233> become applicable? If so, when? Will there be a phased approach?

USP General Chapter <231> will be omitted once General Chapters <232> and <233> become applicable, with consideration of a reasonable period of time for manufacturers to meet the new requirements.

10. Will General Chapter <231> still be applicable in monographs where cited? Will it still be applicable in monographs for veterinary articles where cited?”

Chapter <231> still is applicable where cited in monographs. Although General Chapter <232> indicates that veterinary products are exempt from the new general chapters’ requirements, many monographs for veterinary articles still require conformance to General Chapter <231>. The responsible Expert Committee for these monographs is working with interested stakeholders, including FDA, to consider future options.

11. Can manufacturers work with USP on a specific product that may not meet the limits of a particular element?

USP hopes to work with FDA and with individual manufacturers on resolving scientific issues arising from the new Elemental Impurities requirements, again balancing manufacturer interests with public health impact.

Revision History:

Version 2: June 7, 2013

- Added FAQs
 - 'What is a "deferral" and what are the possible outcomes?'
 - 'How will the Advisory Group be formed? Who will be its members?'
- Revised FAQ
 - Will General Chapter <231> still be applicable to veterinary monographs?
- Omitted FAQ
 - "What does USP plan to do with other general chapters that address elemental impurities such as <251> Lead, <211> Arsenic and <261> Mercury, etc.?"

Version 1: May 29, 2013

- Initial version posted