Frequently Asked Questions Regarding the Implementation of USP General Chapters <232> Elemental Impurities—Limits, <233> Elemental Impurities—Procedures, and <2232> Elemental Contaminants in Dietary Supplements

Version 4: January 14, 2015

1. How will General Chapters <232> Elemental Impurities—Limits and <2232> Elemental Contaminants in Dietary Supplements become applicable to monographs? Will they apply to all monographs or just to drug products?

   General Chapters may be applied by reference in a monograph, by reference in an already applicable general chapter, or by a statement in General Notices that specifies their broad applicability. USP will apply General Chapters <232> and <2232> to monographs via *General Notices* provision 5.60.30 *Elemental Impurities in USP Drug Products and Dietary Supplements*. General Chapter <232> will apply to drug products currently in the *USP–NF.* General Chapter <2232> will apply to finished dietary supplement dosage forms. The General Chapters also could be made applicable by reference in any monograph on a case-by-case basis.

2. When will conformance to General Chapters <232> and <2232> be required?

   As specified in the Notice of Intent to Revise for General Notices 5.60.30 posted on January 14, 2015, USP anticipates that *General Notices* 5.60.30 *Elemental Impurities in USP Drug Products and Dietary Supplements* will specify January 1, 2018 as the date that General Chapters <232> and <2232> will become broadly applicable to drug products (<232>) and finished dietary supplement dosage forms (<2232>) in the *USP–NF*. Only in the event that a monograph specifically references one of these General Chapters could they be required prior to January 1, 2018, and then only for the article covered by that specific monograph.

3. Are General Chapters <232> Elemental Impurities—Limits, <233> Elemental Impurities—Methods, and <2232> Elemental Contaminants in Dietary Supplements currently official?

   General Chapters <232> and <233> became official February 1, 2013; General Chapter <2232> became official August 1, 2013. Until *General Notices* 5.60.30 *Elemental Impurities in USP Drug Products and Dietary Supplements* makes the General Chapters applicable on January 1, 2018 as anticipated, however, these General Chapters would necessarily be applicable only if they are referenced in a particular monograph.

   It is important to note that USP intends to revise General Chapters <232> and <233> with changes related to the ICH Q3D Step 4 document as well as other editorial changes. General Chapters <232> and <233> will remain official in their current form until the revisions become official, likely in *Supplement 2* to *USP 38–NF 33* (December 1, 2015).

4. Why doesn't *General Notices* provision 5.60.30 *Elemental Impurities in USP Drug Products and Dietary Supplements* reference General Chapter <233> Elemental Impurities—Procedures?

   General Chapter <233> will be made applicable by being referenced in General Chapters <232> and <2232>, and thus does not need to be referenced separately in

General Notices 5.60.30. General Chapter <233> already is applicable in certain cases through reference in currently official monographs (see question 1).

7. Will General Chapter <231> be omitted once General Chapters <232> and <2232> become applicable?

   General Chapter <231> will be omitted once General Chapters <232> and <2232> become applicable on January 1, 2018. The removal of references to <231> from *USP–NF* monographs also will be official as of January 1, 2018.

8. Can I implement General Chapter <232> or <2232> in advance of January 1, 2018?

   In the proposed revision to *General Notices* 5.60.30, USP intends to indicate that early adoption of General Chapters <232> and <2232> will be permitted by USP. This would provide flexibility for users to implement the new requirements at a timing that is appropriate for their specific cases, and in such cases relieve such products and any constituent ingredients of having to conform to <231>. Given that General Chapters <232> and <2232> provide significant improvements over existing approaches in the control of elemental impurities, USP encourages users to implement the new methods as soon as reasonably possible.

9. 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, balancing manufacturer interests with public health impact. Upon receipt of the appropriate supporting information, USP may propose a revision to the monograph to address its special requirements. Such requirements in a monograph, should the monograph be approved and become official, would take precedence over the requirements specified in <232> or <2232>.

Revision History:

Version 4: January 14, 2015

- General revisions to FAQs as part of the announcement of the January 1, 2018 date of applicability of General Chapters <232> and <2232>
- Added FAQ
  - ‘Can I implement General Chapter <232> or <2232> in advance of January 1, 2018?’
- Deleted FAQ
  - ‘Why is USP’s revision to General Chapter <232> not fully aligned with the limits specified in the ICH Expert Working Group Q3D Step 2b draft?’, as USP anticipates alignment with the limits specified in ICH Q3D Step 4

Version 3: December 27, 2013

- General revisions to FAQs as part of the announcement of the December 1, 2015 date of applicability of General Chapters <232> and <2232>

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