

Elemental Impurities– An Update

Kahkashan Zaidi, Ph.D.
Veterinary Drugs Stakeholder Forum
February 19-20, 2014

- ▶ Introduced in USP VIII (1905)
 - Consists of three procedures, all involving
 - Sulfide precipitation of metals
 - Visual comparison to lead standards

- ▶ Methods in the EP and JP are similar to the USP methods

- ▶ USP efforts to revise <231> started in 1995

Three Chapters to address:

- ▶ Metals of concern and their limits in pharmaceuticals (General Chapter <232>)
- ▶ Methodology for assessing the levels of metals present (General Chapter <233>)
 - Two compendial procedures
 - Procedure acceptance criteria for alternative procedures
- ▶ Separate Chapter for dietary supplements, <2232>
 - Addresses speciation (toxic vs. nontoxic forms of As, highly toxic form of Hg, occurring in botanicals and fish-based products but seldom in pharmaceuticals)

- ▶ USP approach to elemental impurity control is **both health based and risk based**
- ▶ Control metals that are toxic
- ▶ At limits that are toxicologically relevant
- ▶ At all times during a drug product's shelf life
- ▶ With a risk-based approach as to what and when to test

▶ Applies to drug products

- Drug substances
- Excipients

▶ Does not apply to dietary supplements

▶ Does not apply to Veterinary products

- *The limits indicated in this chapter are not required for articles intended only for veterinary use* and conventional vaccines.
- Requirements listed in this chapter also do not apply to total parenteral nutritious (TPNs) and dialysates.

- **Dec 27, 2013**--Revised chapters <232> and <233> on Elemental Impurities **posted on the USP website**
 - Partial alignment of chapter <232> with the ICH Q3D Step 2 limits
- Will also be published in **Pharmacopeial Forum 40(2)** – Comment deadline of May 31, 2014.

Implementation of Elemental Impurities

- ***Supplement 2 to USP 38—NF 33 with an official date of December 1, 2015.***
 - ➡ Implementation of Chapters <232> and <2232>
 - ➡ Omission of chapter <231> Heavy Metals
 - Chapter <231> omission proposal was published in PF 39(1)
 - ➡ Removal of all references to General Chapter <231> Heavy Metals from monographs and general chapters in the *USP—NF*



Questions