# USP Stimuli Article Future of Element - Specific Chapters in the *USP–NF*

Multiple stakeholders; **one objective.**


International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

# Future of Element-Specific Chapters in the *USP–NF*

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# Removal of Specific Element Requirements from Monographs

# View point from Excipient and Pharmaceutical Industry

# USP Stimuli Questions

- What will be the future of *USP* chapters that provide specific information regarding the analysis of individual elements, such as arsenic (As) *Arsenic* ⟨211⟩, lead (Pb) *Lead* ⟨251⟩, selenium (Se) *Selenium* ⟨291⟩, mercury (Hg) *Mercury* ⟨261⟩, and others?
- What about *USP* monographs that may have limit tests for specific elements and refer to their respective element-specific chapters for methodology?

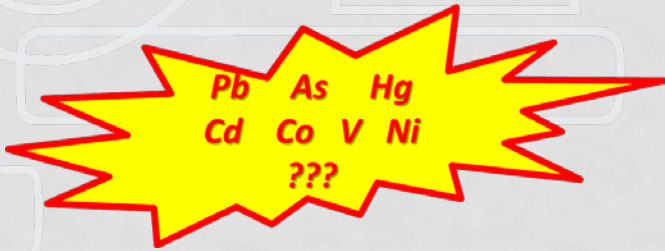
# Stimuli Questions

- What about *USP* monographs that include limits for specific elements that differ from the limits established in ⟨232⟩?
- Limit tests and references to element specific chapters are included in about 1000 monographs.
  - **Excipients = 150**
  - **Drug Substances/Drug Products = 272**

# Industry Concerns
# Specific Element Requirements in Monographs

- Pharmacopeias should **not** change an existing monograph specific element requirement (methods/limits) unless evaluated as part of an individual monograph modernization activity designed to include specific metal requirement.

- Existing element limit requirements and test methods **should stay in the monographs and not be removed** – to allow for comparisons with historical methods/data



# Industry Concerns
# Specific Element Requirements in Monographs

- **History supports limits/test methods which can be used in risk assessments as worst case examples AND provide useful information to users since actual detailed information is limited.**

- **No changes should be made to the limits and no new elements should be added based on a limited amount of batch testing, since excursions won't show up except over long-term history**

# Industry Concerns
# Specific Element Requirements in Monographs

- Current monograph limits and test methods are linked, USP should not change the monographs to use the approaches for methodology and analysis in <233> or the existing limits unless validation work conducted demonstrates that the current methods in the monograph and any alternative methods give equivalent results.

# Industry Concerns
# Specific Element Requirements in Monographs

- Veterinary applications: VICH did not sign on to Q3D.  With the deletion of GC <231> and specific elements from the API/excipient monographs, there is a concerns that this is creating risk for the Animal Health Industry.

# Industry Concerns
# Specific Element Requirements in Monographs

- API suppliers: Elemental Impurities is for the finished drug product not the Drug Substances.
- Removing specific metal tests from USP would impact API supplier,  FDA would not allow deletion without justification.

# Industry Concerns
# Specific Element Requirements in Monographs

- EDQM announced actions:
  - Test for heavy metals (method 2.4.8) will be deleted from all individual monographs except from monographs of substances for veterinary use only (9th edition).
  - Other tests for specific EIs in individual monographs will be reviewed by groups of experts on a case by case basis. Secretariat provided lists of monographs concerned to the groups.
  - Specific tests in individual monographs for elements not covered by ICH Q3D will remain untouched but maybe considered upon discussion of a monograph in the group.

# Industry Concerns
# Specific Element Requirements in Monographs

- **EDQM - Options for consideration of test on Specific EI**
  a. Delete all tests for specific EIs from individual monographs.
  b. Keep tests for EIs with limits justified higher than the PDE. Delete all other tests.
  c. Delete all tests for specific EIs from individual monographs of synthetic organic substances (unless option b. applies). Keep tests for EIs in individual monographs of inorganic substances or natural products (tests for natural contaminants).

Information from EDQM meeting in Tallin, Sept. 2016

# Industry Concerns
# Specific Element Requirements in Monographs

- **EDQM - Options for consideration of test on Specific EI**
  - d. Delete all test for intentionally added EIs from all monographs (unless option b. applies) and keep all other tests.
  - e. Keep all tests for specific EIs in individual monographs; introduce new tests if necessary.

**There are Pros and Cons for each option**

Information from EDQM meeting in Tallin, Sept. 2016

# Industry Concerns
# Specific Element Requirements in Monographs

- If, after significant assessment, a decision is made to update or change the monographs in any way, USP, Ph.Eur. and JP should **harmonize** regarding which elements should remain in the monographs along with their appropriate limits.

# Industry Concerns
# Specific Element Requirements in Monographs

- **Collaboration** with a multiple global excipient manufacturers to supply historical data currently used to support commercial drug products **is essential** in the assessment and establishment of limits, which should take into consideration the market and process knowledge of the excipient manufacturers.

- It is critical not to make changes which could impact the acceptability of excipients

  - **Excipients do not represent any significant risk on their own!**

# Questions for Discussion

- What will be the Major Impact of removal of specific metals tests from Excipient, Drug Substance and Veterinary products monographs

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# Questions for Discussion

USP needs to evaluate each monograph individually with industry to determine if the specific metals test is needed based on historical data.

- What type of information is available from industry and will it be shared

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# Your Questions – Thank You!