Use of Literature and Database Information – A Regulator View

PQRI/USP Elemental Impurities November 2017
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Acknowledgement and Disclaimer

- This presentation is based on discussions within the ICH Q3D EWG and IWG, within the QWP as well as the experience from actual submissions assessed by the Swedish MPA
- Nevertheless, the views expressed in this presentation represents the view of the author. They are not necessarily reflecting the opinion of the ICH, the QWP or the MPA

Risk Assessment – Core of Q3D

- Compliance with ICH Q3D should be ascertained by testing when necessary
- The described Risk Assessment is the tool establish when testing is necessary or not
- Should be based on scientific knowledge and an understanding of the product
- The Guideline envisage the potential use of other sources of information than what is generated within the Company

Q3D – Sources of Information

- Section 5
  - *Information for this risk assessment includes but is not limited to: data generated by the applicant, information supplied by drug substance and/or excipient manufacturers and/or data available in published literature.*
- Section 5.5
  - *The data to support this risk assessment can come from a number of sources that include, but is not limited to:*
    - *Prior knowledge;*
    - *Published literature*
    - etc.

Knowledge on Elemental Impurities in Excipients

- During the work of the EWG it was noticed that
  - only some pharmacopoeial monographs contained limits on elemental impurities
  - the available knowledge on typical levels of elemental impurities in excipients were very limited.
  - the willingness to investigate their products and share their results was varying from excipient supplier to excipient supplier

Wider Knowledge on Elemental Impurities in Excipients

- There was a strong feeling that the publication of the Guideline would stimulate
  - academic screening and research
  - industry investigations
  - pharmacopoeial activities
- Eventually more extensive knowledge would became available

What has Happened so Far?

RESEARCH ARTICLE – *Pharmaceutics, Drug Delivery and Pharmaceutical Technology*

Elemental Impurities in Pharmaceutical Excipients

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Received 14 May 2015; revised 26 August 2015; accepted 28 August 201
Published online 23 September 2015 in Wiley Online Library (wileyonl

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Collaboration & Data Sharing > Elemental Impurities

Collaboration & Data Sharing

- AI/PDE
- Aromatic Amines
- Elemental Impurities

Elemental Impurities

The Elemental Impurities project is a collaborative data-sh
pharmaceutical industry, in partnership with Lhasa Limited

This collaboration is designed to share analytical data on t

Use of Literature and Database Information in Applications

- The experience of the MPA in current application is
  - Frequent use of literature references regarding packaging material (Jenke et al.)
  - Some examples of the use of literature references regarding excipients (Li et al.)
  - No use of references to other compilations of data such as Lhasa.

Regulators View on Database Information

- Companies sharing and pooling data on elemental impurities found in excipients is very interesting
- Contributes to a build up of an understanding of the presence of elemental impurities in excipients
- Increases the confidence in the anticipation that excipients normally do not constitute a great risk
- Identifies those (e.g. mined) excipients that may be of concern and estimates the magnitude

Regulators Views on the Role in a Dossier

- Database information on elemental impurities
  - Supports the company's risk assessment
  - Will currently not be sufficient as a standalone justification for not testing
  - May allow for not having to test in the control strategy based limited in-house analyses (fewer batches)
- Whether such data will be sufficient as standalone justification for not testing (at least for some excipients) in the future remains to see

Regulators Assessment of Database Information

- How transparent can/will companies be, referring to such data?
  - Differences in grades
  - Differences in manufacturing methods/source
  - Number of batches tested
  - Number of suppliers tested
  - Mean values vs. Min/Max
  - Validation of the analytical methods
  - Method of digestion

Regulators Assessment of Database Information

- How much does the size of the database mean to the usefulness of the data?
- In a Risk Assessment, the closer your observed or predicted levels come to the Control Threshold or the PDE, the more important will actual data on your own material be.

Summary

- Published literature as well as databases with compiled data on elemental impurities in different excipients will be very valuable to increase the scientific understanding
- Currently this is not yet sufficient as standalone justification for omitting testing, but certainly supporting that
- Whether this may change with more data being compiled remains to see
- Can regulators in the future gain access to such databases?
  - To enhance their knowledge and confidence

Thank you!