Sharing elemental impurity data for excipients aids ICH Q3D risk assessments

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Introduction

In 2014 the International Council on Harmonisation (ICH) established a new elemental impurity (EI) quality guideline that applies to all drug products [1]. ICH Q3D is predicated on risk assessment [2], rather than the absolute confirmation that the 30% permitted daily exposure (PDE) or control threshold will never be exceeded. If the risk assessment fails to demonstrate that an EI level is consistently below the control threshold, then controls need to be established to ensure the EI level does not exceed the PDE.

The first step of the risk assessment involves the identification of known and potential sources of EIs. For the second step of EI evaluation, ICH Q3D states that sources including published literature are suitable for the support of risk assessments. This poster demonstrates how a database of shared excipient EI determinations [3], with equivalent provenance to published literature, can additionally be used as a source of information.

Method

A consortium of pharmaceutical companies with an interest in the sharing of EI data for excipients was established in 2015. Lhasa Limited acts as the honest broker and hosts the data in a custom Vitic Nexus® database [4]. Information regarding excipient supplier and batch is appropriately blinded by Lhasa Limited - it is expressly not the intention that the database should be used to select suppliers based on reported EI levels or their variability - but full access to standardised excipient names and their corresponding EI profiles is provided.

Results

To date the consortium comprises 15 pharmaceutical companies and the data within the EI database continues to grow due to regular donations from consortium members. Two excipient suppliers have also shared data and the database currently contains the results of 27,913 elemental determinations for 216 excipients. It represents the largest known collection of data of this type. The high quality of the data is evidenced by the observation that 99% of the analytical studies include complete information on the sample preparation and analytical methods used as well as the validation approach taken.

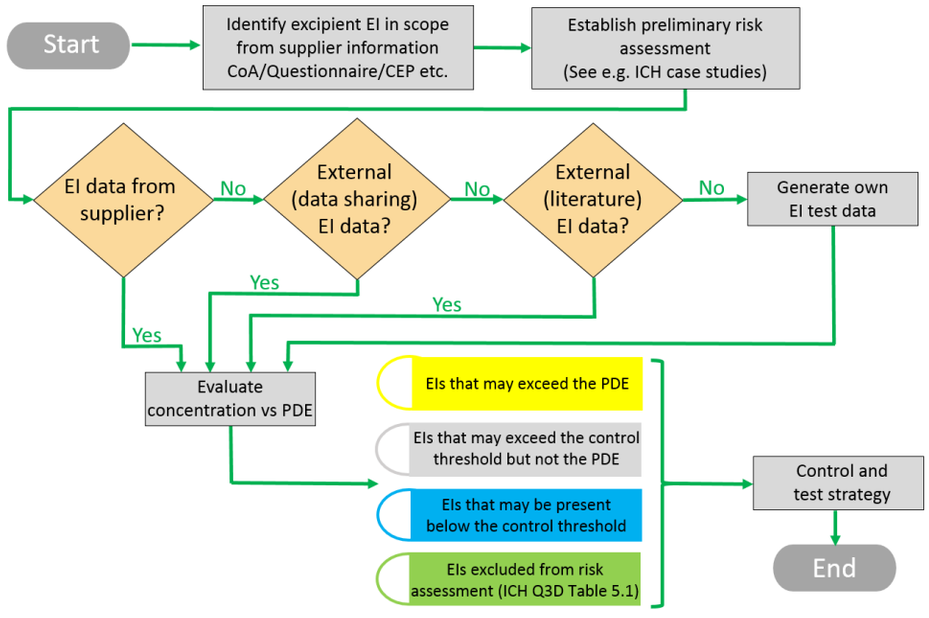

Figure 1: Risk assessment workflow incorporating the use of shared EI data.

Results (continued)

The workflow in Figure 1 illustrates how data in the EI database can be used to aid ICH Q3D risk assessment. Figure 2 shows how relevant information is retrieved from the database:

1. For excipient EIs identified in scope in step 1 of the risk assessment and for which no, or insufficient data are available from the supplier, perform a search of the EI database for the excipient by name. Searches can be restricted by the elements or element classes of interest if desired (Figure 2, Search).

2. Review the EI data available for the excipient in the Summary data table (Figure 2, Review). This includes summary statistical parameters such as mean, minimum and maximum concentrations (µg/g). Further detailed information on each analytical study, including method, can be accessed if required.

3. Export the EI data from the database in a suitable format (Figure 2, Export) for incorporation into risk assessment calculations and the resulting detailed report. Submit summary risk assessment conclusions in the normal way.

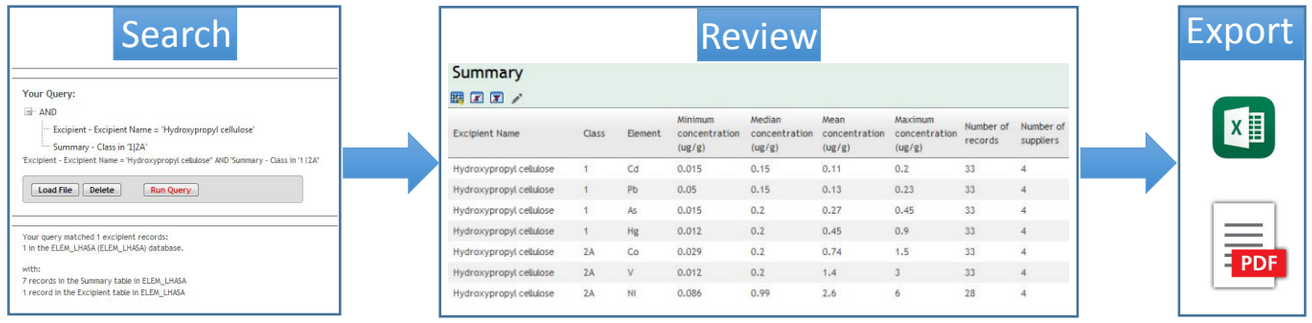

Figure 2: Example of EI database search page, the summary table data for class 1 and 2A elements and two options for export format associated with Hydroxypropyl cellulose (data for other elements not shown).

Conclusion

The use of shared EI data allows more informed judgements during the evaluation phase of an ICH Q3D risk assessment. The EI database represents the largest known collection of data of this type. In the short-term, supportive drug product testing may be used to confirm conclusions of low risk and ensure that appropriate controls have been established. In the longer term, it is envisaged that drug product testing itself will be less frequently required under certain circumstances (*e.g.* for oral drug products where sufficient data exist to support a conclusion of low risk). Therefore increasing the visibility of data in the database will assist in the overall understanding of EI levels and aid risk assessments.

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References

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