Final Concept Paper
Q3D: Elemental Impurities EWG for the Cutaneous and Transdermal Route
dated 1 September 11 2016
Endorsed by the ICH Management Committee on 15 September 2016

Type of Harmonisation Action Proposed

Establishment of an Expert Working Group (EWG) to develop Permitted Daily Exposures (PDEs) levels for Elemental Impurities (EI) for products administered by the cutaneous and transdermal routes of administration.

Statement of the Perceived Problem

ICH Q3D Elemental Impurities is a quality guideline for the control of elemental impurities in new drug products (medicinal products). ICH Q3D was finalised in December, 2014 and establishes PDEs for 24 EIs for drug products administered by the oral, parenteral and inhalation routes of administration. In addition, guidance is provided in Q3D on how to develop an acceptable level for EIs for drug products administered by other routes of administration. Training material to assist in the implementation of Q3D has been finalized and Training Modules 0-9 are currently available at ich.org.

During the course of preparing the *Step 4* Q3D Guideline, interest was expressed by industry in developing PDEs for EIs for products administered on skin and its appendages (e.g., hair, nails); these products remain the largest area where PDEs for EIs have not been established. Cutaneous and transdermal PDEs were not developed at that time due to the late request for inclusion (post *Step 2*). These products include both prescription and over-the-counter products. It is possible that different levels of EIs could be deemed acceptable by regulators in the different ICH and non-ICH regions in similar products due to the information in the risk assessment provided to regulators, leading to a lack of harmonisation. In addition, since the intact skin serves as a barrier to absorption, it is possible that not all EIs in Q3D will require cutaneous and transdermal PDEs, streamlining the risk assessment process for these products. To continue the process of harmonisation, it would be beneficial to develop PDEs for products administered to skin and its appendages, where necessary.

Issues to be Resolved

A summary of the activities and outputs which need to be addressed include:

- Determine which EIs will need to have a safety-based PDE;
- Use methodology described in Q3D to develop the PDE.

Type of Working Group and Resources

The EWG will be comprised of experts from each of the Founding Regulatory Members and from other ICH Members as appropriate. Additionally, ICH Observers may participate on the EWG pending a favorable decision by the ICH Assembly. The focus of the EWG will primarily be a safety assessment by toxicologists. Given the depth and breadth of experience of the current Implementation Working Group members (IWG), it is recommended that the EWG membership be drawn from the current IWG.

Timing

Agreement of Concept Paper by the Q3D EWG	September 1, 2016
Adoption of Concept Paper by the ICH Management Committee	September 15, 2016
Completion of development of PDEs	12-18 months

One face-to-face meeting may be needed.