

Final Business Plan
Q3D: Elemental Impurities IWG
dated 1 October 2014

Endorsed by the ICH Steering Committee on 21 October 2014

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

ICH Q3D Elemental Impurities is a guideline developed to provide a global policy for controlling elemental impurities in drug products. The process and principles described in ICH Q3D build upon the science and risk based principles described in Pharmaceutical Development (ICH Q8) and Quality Risk management (ICH Q9). Experience with the risk management concepts outlined in ICH Q8, Q9, Q10 and Q11 has demonstrated that there are still significant challenges in aligning interpretations and approaches in implementation. In the period after approval of ICH Q8-Q11, it became evident in that even with well accepted language and concepts contained in the guideline, the lack of familiarity and common interpretations of risk based approaches had the potential to create divergent opinions across the ICH and non-ICH regions. As a result, Implementation Working Groups (IWGs) were formed to provide implementation support and training materials to provide clarification and ensure appropriate interpretation and implementation of the original guidelines in the ICH regions and several non-ICH regions.

During the development of ICH Q3D, the EWG solicited broad input from constituents from participating organisations using several different tools (including surveys and full document reviews) which resulted in the creation of a consistent guideline. However, the comments and questions raised in the public comment period, demonstrated a lack of harmonised understanding of some of the key principles and in particular the application of risk-based approaches and the use of risk assessments. We propose the formation of an IWG for Q3D to develop training materials and supporting implementation aids. The goal of the IWG is to maximize the efficiency of implementation by fostering aligned interpretations of the Q3D Guideline in ICH and non-ICH regions alike.

- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with “non action”?*

The potential for variability of interpretation is high (based on the current experience with ICH Q8-Q11). This has the potential to require multiple iterations of dossier review and propagate multiple standards across ICH and non-ICH regions. By providing implementation aids and training materials, the differences in interpretation can be reduced, which will have a positive impact on both preparation and review of submission dossiers.

2. Planning

- *What are the main deliverables?*

The primary deliverables for the IWG are:

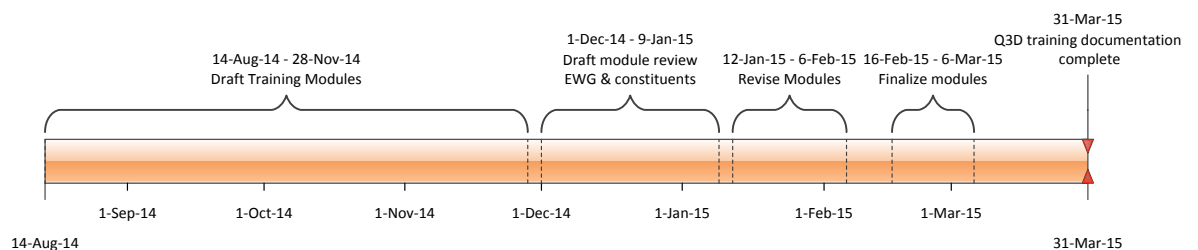
- Training presentations including:
 - General overview of the guideline
 - Example(s) of the execution of risk assessment(s)
 - Example(s) of application of the guideline to less than daily dosing
 - Example(s) of application of the guideline to other routes of administration
- Frequently Asked Questions (FAQs) document (providing answers to the most often asked questions received during the public comment period);
- Example document providing an approach to documenting the information and data supporting the risk assessment to be presented in a regulatory submission;
- Expert support to the roll out of the training programme (through workshops and/or preparation of web based sessions) in ICH and non-ICH regions.

- *What resources (financial and human) would be required?*

By providing the training and implementation aids, a harmonised approach can be introduced and sustained. The IWG should be constituted by members from EU, EFPIA, FDA, PhRMA, MHLW, JPMA, Health Canada and Swissmedic. One member can also be nominated by WHO Observer, the 3 regions’ Pharmacopeias, biotech industry, WSMI, IGPA, IPEC and APIC as well as RHIs, DRAs/DoH (if requested). It is envisioned that most of the work of the IWG will be conducted via electronic formats (document exchange or review and teleconferences). In order to finalise the training documents, it is recommended to hold one face to face meeting (which could be at a time separate from the next ICH twice yearly meeting).

- *Timeline and Milestones*

Agreement of Concept Paper and Business Plan by the Q3D EWG	October 3, 2014
Adoption of Concept Paper and Business Plan by the ICH Steering Committee	October 21, 2014
Establishment of the ICH Q3D IWG	October 31, 2014
IWG meeting to finalise training materials	1Q 2015
Training materials finalised	March 31, 2015



3. The impacts of the project

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*
 - Aligned interpretation of the fundamental principles underlying the guideline – starting with the initial approval and implementation of the guideline;
 - Provision for additional implementation support for all regions (of significant importance to non-ICH regions which have less experience in the background development of the guideline);
 - Leverage of the existing EWG experience and knowledge base (simplified transition from EWG/IWG); maintaining momentum and an ability to commit to an aggressive timeline.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

The proposed training materials are consistent in the approach that has been received favorably for ICH Q8-Q11. One significant difference is to establish the IWG shortly after step 4 sign-off to create the training materials concurrent with the implementation timeline to ensure a smooth implementation.

4. Post-hoc evaluation

- *How and when will the results of the work be evaluated?*

The following training elements, as key deliverables, are proposed for consideration of and creation by the IWG:

- General overview of the guideline
- Considerations for other routes of administration
- Considerations for justifying levels higher than the PDE (short term use, less than daily dosing)
- How to develop an acceptable intake for an element not in the guideline
- Considerations for Large Volume Parenteral Products
- Execution of the Product Risk Assessment
- Control Strategy Development
- Calculation Options
- Product Assessment Case Study
- FAQs (Based on most prevalent public comment questions)

The success of the IWG will ultimately be measured by the smoothness and harmony of implementation among regions. Intermediate metrics will include completion of all presentations in the specified timelines, and the development of training schedules in ICH and non-ICH regions. The training materials will be made available through the ICH website.