

Final Business Plan
Q11: Q&As on Selection and Justification of Starting Materials for the Manufacture of Drug Substances

Focus on chemical entity drug substances

dated 31 October 2014

Endorsed by the ICH Steering Committee on 10 November 2014

1. The issue and its costs

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

Interpretation of the high level principles in ICH Q11 for the selection and justification of starting materials is not fully aligned between and within regulatory bodies and industry. Further discussion on the specific areas of divergent interpretation and subsequent clarification will benefit harmonisation in this area.

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

A basic principle in the assurance of quality of drug substance is manufacturing within the framework of Good Manufacturing Practice (GMP). If starting materials are not appropriately defined, GMP may not be applied appropriately. Equally, inclusion of those synthetic steps which represent minimal risk to the quality of the drug substance in the regulated process adds burden to industry due to the need to comply with GMP and maintain the regulatory dossier over the lifecycle of the product. Selection of appropriate starting materials could be improved by providing further clarity on the criteria used to define and justify the starting materials for the drug substance.

Industry:

Currently, industry uses various strategies to address starting material challenges in anticipation of divergent global regulatory expectations (e.g., validating manufacturing steps that have no significant impact on drug substance Critical Quality Attributes (CQAs); evaluating every step of the process for known and potential impurities with equal intensity; application of GMP unnecessarily early in the manufacturing process; registering long processes irrespective of control strategy and what steps impact drug substance quality). These strategies significantly increase development and production costs but have little value in assuring quality and patient safety.

Regulator:

Regulator resources are impacted because regulators spend considerable time confirming acceptability of a proposed starting material, especially if inadequate information is provided in the marketing application. The need for extensive dialogue during review of marketing applications would be considerably reduced or eliminated if the expectations of regulators and industry were more closely aligned.

2. **Planning**

- *What are the main deliverables?*

A Q&A document will be developed to clarify ICH Q11 selection principles and thereby achieve more consistency in the outcomes of starting material (and control) proposals. The IWG will develop the Q&A based on information already available from public workshops, consortiums, and white (reflection) papers that have been held or published since the finalisation of ICH Q11.

The main deliverables are:

- *Step 2a/b* Q&A document by the ICH meeting in November 2015;
- *Step 4* Q&A document (to be determined);
- Regular progress updates to the Steering Committee, upon request.

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

The working group should include representatives from the ICH official members (EU, EFPIA, FDA, PhRMA, MHLW, JPMA, Health Canada and Swissmedic). One member can also be nominated by WHO Observer, EDQM, WSMI, IGPA, and API industry as well as RHIs, DRAs/DoH (if requested).

The team would primarily work virtually via email and other telecommunications. However, due to the short timeline for completion, it is anticipated that consensus building on the contents of the future Q&A would most likely require the IWG to meet at least once in the form of a face-to-face meeting. It is proposed that the IWG revisit the need for a face-to-face meeting and identify a date, if needed, based on topics that require more in-depth discussions.

- *Timeline and Milestones*

Adoption of Concept Paper by Steering Committee	November 10, 2014
At minimum, monthly telecons starting	November 17, 2014
Face-to-face	TBD
<i>Step 2a/b</i> document to present to SC	November 2015
<i>Step 4</i> document sign-off	TBD (depends on the need for public comment)

3. **The impacts of the project**

Clarification of the principles about selection and justification of starting materials described in ICH Q11 will allow for better alignment in interpretation between and within industry and regulatory bodies. This will lessen the burden on regulators and industry alike, and reduce the potential for delays in the approval of drugs related to starting materials.

4. **Post-hoc evaluation**

The evaluation of this Q&A on the selection and justification of starting materials will be considered within the ICH Q11 *post-hoc* plans since these already include starting material evaluations.