Final Concept Paper

Q13: Continuous Manufacturing of Drug Substances and Drug Products

Endorsed by the Management Committee on 13 January 2023

Documented dated 21 December 2022

Type of Harmonisation Action Proposed

Establishment of an Implementation Working Group (IWG) to prepare and deliver a training programme (with associated materials) facilitates an aligned interpretation and a harmonized implementation of ICH Q13 in ICH and non-ICH regions. The intent of this IWG is not to provide comprehensive training on all aspects of continuous manufacturing (CM) but rather to illustrate the application of specific concepts or principles of Q13.

Statement of the Perceived Problem:

ICH Q13 Continuous Manufacturing of Drug Substances and Drug Products is a Quality guideline that provides scientific and regulatory considerations for the development, implementation, operation, and lifecycle management of CM processes. Current pharmaceutical manufacturing processes are based on batch processes, while CM is an advanced manufacturing concept that is unfamiliar to both pharmaceutical industry and regulatory organizations across multiple regions. CM could offer several potential advantages over conventional batch manufacturing in terms of ensuring consistency of product quality, meeting patient needs, and enabling a rapid response during public health emergencies.

The Q13 guideline discusses novel concepts and scientific approaches relevant for CM and includes several new or modified regulatory approaches that are applicable across multiple regions. Global alignment on scientific and regulatory approaches is critical to enable the adoption of this new technology and realize the full benefits offered by CM. The Q13 guideline builds on the concepts articulated in existing ICH guidelines such as Pharmaceutical Development (ICH Q8), Quality Risk Management (ICH Q9), Pharmaceutical Quality System (ICH Q10), and Development and Manufacture of Drug Substances (ICH Q11). The Q13 guideline also references ICH Q12 guideline for lifecycle management of CM. Several novel concepts articulated in Q13, as well as the implementation of Q13 within the framework of Q8-Q12 and the regulatory frameworks in the various ICH regions, require more detailed clarification. In addition to the foreseen need for training in the ICH Q13 Business Plan, feedback received during the Q13 public consultation period also underscores the need for further support regarding the implementation of Q13. Additional training materials are required to address the different level of understanding of key scientific and regulatory concepts amongst regulators and industry stakeholders.

Development of multi-faceted training materials and approaches (e.g., presentations, video, industry-led training, regulator-only training, in-person training at CM facilities or laboratories when possible) enables detailed dissemination and discussion of CM concepts and provide an opportunity for inclusion of practical examples to illustrate how Q13 can be applied to the development, routine operation, and lifecycle management of CM processes. This level of detail is impractical for inclusion in an ICH guideline. It is noted

that ICH Q8-Q12 benefitted significantly through the preparation and distribution of detailed training materials and implementation aids to further clarify new concepts.

Issues to be Resolved:

The following outputs and activities should be addressed:

a. Training materials to:
   - Illustrate the general concept of CM process operation (e.g., through animation and/or video)
   - Provide detailed clarification of novel scientific concepts and regulatory expectations pertinent to CM (e.g., through practical examples)
   - Expand discussion of Annex I-V in Q13 to address some specific CM implementation aspects relevant for different modalities

b. Expert support to the roll out of the training programme to both regulatory and industry stakeholders in ICH and non-ICH regions through workshops, web-based sessions, and other training mechanisms (e.g., collaboration with relevant stakeholders to provide targeted training such as in-person training at CM facilities or laboratories when possible).

Background to the Proposal:

The Q13 guideline provides a harmonized framework that is broadly applicable for the range of products covered under the guideline's scope. While the guideline includes CM examples for different modalities, it cannot always provide detailed explanations or address specific implementation aspects to illustrate how Q13 could be applied to the broad range of products under its scope. The CM experience across different regions is currently limited and varied. During the development of the guideline, external and internal stakeholders and interested parties clearly communicated the novelty and complexity of the concepts described in the Q13 guideline. The constituent reviews and feedback received during the public consultation period illustrated the varied levels of understanding of key concepts and implementation aspects by the stakeholders. Notably, implementation of Q13 within the pharmaceutical quality management system and lifecycle management of CM were areas of variable interpretation or lack of understanding. Industry and regulatory organizations in many regions will need to take additional steps to implement the Q13 concepts, including staff training, ideally before Q13 implementation in each region. Therefore, availability of training materials provides a critical resource to both regulators and industry implementing the Q13 guideline.

The development of a comprehensive training programme and supporting documentation sponsored by ICH is essential to ensure the proper interpretation and aligned understanding of Q13 by both industry and regulators. It is envisioned that the CM training include a short video to demonstrate this new technology as well as additional documents, presentations, and if possible, in-person training at CM facilities or laboratories. These collectively provide more clarity, remove ambiguities, and address specific details relevant to CM modalities. To promote wider use of CM, the roll out of training materials and/or programmes is expected to occur not only in ICH regions, but also in non-ICH regions. The formation of an

IWG for development and delivery of training materials provides an effective mechanism to enable harmonised implementation of Q13 on a global basis.

Type of Expert Working Group Recommended:

Given the expertise of the current EWG members and their familiarity with regulatory framework in individual regions, it is recommended that the IWG membership be the same as the current Q13 EWG. Subgroups will be formed to develop the materials and training approaches through email, teleconference and in-person meetings. The subgroups will obtain input from the entire IWG through discussions via email and teleconferences.

Indicate if the scope of activities of the Working Group would warrant expertise from any of the following fields:

□ Advanced Therapy Medicinal Products

□ Bioequivalence Studies

□ Biostatistics and clinical trial methodology

X Biotechnology-derived products

□ Electronic standards or technical considerations

X Generics

X Good Manufacturing Practices

□ Non-clinical safety

X Novel dosage forms

☐ Pharmacogenomics

☐ Pharmacovigilance

□ Pediatrics

□ Post-marketing clinical trials

□ Pre-marketing clinical trials

X Small Molecules/New chemical entities

□ Therapeutic area-specific Safety/Efficacy (please specify):

□ Vaccines

X Other (please specify): Inspection staff (if this is not already captured under the above field of GMP) and Subject Matter Expert in biologics

Timing:

Agreement of Concept Paper by the Q13 EWG	December 2022
Adoption of Concept Paper by the ICH Management Committee	January 2023
Establishment of the ICH Q13 IWG	January 2023
IWG development of training materials and approach	January 2023 – December 2023
IWG to finalize training materials and approach	June 2024