

Final Business Plan

ICH Q13: Continuous Manufacturing for Drug Substances and Drug Products dated 14 November 2018

Endorsed by the Management Committee on 15 November 2018

1. The issue and its costs

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

The current ICH Guidelines do not sufficiently address technical and regulatory requirements that are unique to Continuous Manufacturing (CM). A harmonised regulatory guideline can facilitate implementation, regulatory approval, and lifecycle management, particularly for products intended for commercialization internationally. This approach will benefit industry and regulators and improve access to medicines.

The proposed new quality guideline will:

- Harmonise CM-related definitions
 - Articulate key scientific approaches for CM
 - Harmonise regulatory concepts and expectations for CM across the regions
- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with “non action”?*

There is a general consensus that continuous manufacturing (CM) has potential for improving the efficiency, agility, and flexibility of drug substance and drug product manufacturing. Regulatory agencies have seen more companies engaged in the development and implementation of CM in recent years than in the past. Although current regulatory frameworks allow for commercialization of products using CM technology, a lack of regulatory guidelines can make implementation, regulatory approval, and lifecycle management challenging, particularly for products intended for commercialization internationally. An ICH guideline would reduce barriers for the adoption of CM technology.

Specific costs from lack of action by ICH include:

- Issuance of final regional guidelines/guidances with differing regulatory expectations.
- Multiple filing strategies required to comply with different regulatory expectations.
- Increased risk and costs for CM implementation due to the lack of harmonised regulatory expectations
- Uncertainty resulting in ad hoc special meetings and consultations between industry and regulators to resolve technical and regulatory questions, and
- Lost opportunities for patients to have improved access to medicines.

2. Planning

- *What are the main deliverables?*

The main deliverable is a new quality guideline, ICH Q13, on continuous manufacturing for drug substances and drug products.

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

The Expert Working Group includes approximately 35 experts. We anticipate the need for six face-to-face meetings and multiple interim teleconferences to complete the new guideline.

- *What is the time frame of the project?*

The new guideline is anticipated to take three years to achieve Step 4, from November 2018 – November 2021.

- *What will be the key milestones?*

The proposed timeline and milestones are below.

- Final concept paper and business plan endorsed: November 2018
- Step 2b: June 2020
- F2F Meeting: June 2021
- Step 4: November 2021

- *What special actions to advance the topic through ICH, e.g. stakeholder engagement or training, can be anticipated either in the development of the guideline or for its implementation?*

The following are potential special actions that may be taken to advance development of the guideline:

- Site-visits to CM facilities (coordinated regionally), for small and large molecules, by regulatory working group members.
- Engage with suppliers to understand technologies' state-of-the-art capabilities
- Presentations at major technical conferences to promote engagement on the ICH guideline during the consultation phase.
- Engagement with external, technical experts.

The following are potential special actions that may be taken to advance or promote implementation of the guideline:

- Creation of formal training materials related to the Q13 guideline and their distribution at inter-agency engagement activities and ICH-supported technical workshops.
- Development of example case studies that cover the breadth of CM applications for distribution with the final guideline and to increase clarity for stakeholders. Small and large molecules manufacturing will be addressed.

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?*

The proposed guideline will harmonise regulatory expectations for drug substance and drug product production using continuous manufacturing, which will increase the likelihood of its implementation by industry internationally. This will result in the following likely benefits:

- Enable the development of new methods for production of new molecules to address therapeutic needs
- Increased manufacturing options available to address public health needs
- Improved access of medicines to patients
- Development of new approaches for the control of drug manufacturing to enhance assurance of quality
- Increase operator safety (process safety risk reductions) for manufacturing
- Reduce resource consumption (for example, materials) and waste generation by shrinking equipment and facility footprints
- Improve the robustness, efficiency, and capability of manufacturing processes

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

The proposed work will assist regulatory bodies internationally. It will identify critical scientific and technical elements to be considered for CM to consistently and reliably manufacture products of the desired quality.

The topic is feasible and implementable from a regulatory standpoint because there is adequate expertise and/or experience to draft a guideline, and pharmaceutical products manufactured with continuous processes have been approved for multiple markets.

- *Will the guideline have implications for the submission of content in the CTD/eCTD? If so, how will the working group address submission of content in the dossier? Will a consult be requested with the ICH M8 working group?*

It is anticipated that any documentation related to CM would be incorporated into the relevant existing CTD/eCTD quality modules. Thus, the guideline would have no implications for the submission of content in the CTD/eCTD. Information may be provided within the guideline on the level of detail and documentation that could be submitted within those sections for CM-related dossiers.

4. Post-hoc evaluation

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

At the conclusion of each stage, we will determine whether deliverables and their timelines were met by comparison against our concept paper and business plan.