ICH Q13
(Continuous Manufacturing)
A Short Update

Nick Lee (ICH Q13 Topic Lead, EC/Europe)

May 2020
In a virtual Stockholm!
Stockholm.... what I had in mind

Dublin... what I’m actually getting!
Need for an ICH Guidance on CM

**Problem statement:** CM is an emergent technology, with significant interest from pharmaceutical and biotechnological companies. One identified barrier to adoption is a lack of harmonisation of regulatory expectations internationally, because current ICH guidelines do not sufficiently address the technical and regulatory requirements that are unique to CM.

**Challenges:** variable maturity of CM technology, harmonisation of operating paradigms, terminology, regional considerations and lifecycle management, amongst others.
Q13 Informal Working Group

Rapporteur: Dr. Sau (Larry) Lee (FDA, US)
Regulatory Chair: Dr. Yoshihiro Matsuda (MHLW/PMDA)

- ANVISA (Brazil)
- BIO
- EC/Europe
- EFPIA
- FDA (USA)
- Health Canada (Canada)
- HSA (Singapore)
- IGBA
- JPMA
- MFDS (Korea)
- MHLW/PMDA (Japan)
- NMPA (China)
- PhRMA
- Swissmedic (Switzerland)
- TFDA (Chinese Taipei)
- IFPMA
- APIC
- IPEC
- National Center, Kazakhstan
- USP
- PIC/S (2019)
- EDQM (2019)
Objectives

Capture key **technical and regulatory considerations** that promote harmonisation, including certain cGMP elements specific to CM.

Provide **guidance to industry and regulatory agencies** regarding regulatory expectations on the development, implementation, and assessment of CM technologies used in the manufacture of drug substances and drug products.

Allow drug manufacturers to employ **flexible approaches to develop, implement, or integrate CM for the manufacture of small molecules and therapeutic proteins** for new and existing products.
November 2018 (1st meeting)

Moved from IWG to EWG

- Finalised the Business Plan, Concept Paper and Work Plan

Developed the draft outline.

Identified key topics, as well as areas of alignment or regional differences.
Concept Paper

Definitions and regulatory concepts

- Definition of CM, different modes of CM, state of control, etc.

Scientific approaches

- Concepts related to control strategy development, system dynamics, sampling, detection and removal of non-conforming material, material traceability, process models, etc.

Regulatory expectations

- Information to include in the dossier; process validation and continuous process verification, and some aspects related to lifecycle management (e.g. conversion from batch to CM).
Guideline Scope

Intended to inform development and implementation of CM for small molecules and therapeutic proteins.

The general CM-related definitions and regulatory concepts therein may also apply to other biotechnological/biological entities.
# Work Plan

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<th>Activity</th>
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<td>Step 1 (Nov2018)</td>
<td>Consensus building and development of the Technical Document</td>
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<tr>
<td>Step 2a/2b (Jun2020)</td>
<td>Consensus on, and adoption of, Technical Document as draft Guideline by Regulatory Members of the EWG</td>
</tr>
<tr>
<td>Step 3 (Jun2020 – Nov2021)</td>
<td>Regulatory consultation and discussion (3 stage process)</td>
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<td>Step 4 (Nov2021)</td>
<td>Adoption</td>
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<td>Step 5 (after Nov2021)</td>
<td>Implementation</td>
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June 2019 (2nd meeting)

Completed the Q13 Outline.

Identified CM facilities in North America, Asia and Europe for site visits by Q13 EWG regulatory members.

Continued consensus building for key scientific and regulatory concepts.

Began drafting the document.
- Four sub-teams formed to begin drafting by teleconference
- Multiple teleconferences to develop and review the content

Completed first draft in October 2019.
November 2019 (3rd meeting)

Further refined the scope and content of three major document sections (Definition and Regulatory Concepts, Scientific Approaches and Regulatory Considerations).

Continued consensus building.

**Identified topics for Annexes**, and developed plans for their drafting.

- Annexes **elaborate and/or provide examples** on the application of some CM topics discussed in the guidance
- Annexes address key aspects associated with **different modalities**
- Annexes provide further information regarding **regulatory expectations**
**Current Status**

**Working draft** of the guideline and annexes issued to EWG for review and discussion within their respective constituencies.

**Annexes** cover...
- Drug substance (NCE)
- Drug product (NCE)
- Integrated drug substance-drug product
- Therapeutic proteins
- Process models
- Managing transient disturbances

**Comments due mid-May**, for collation and distribution to EWG.
COVID-19 Impact on ICH Q13 Development

Step 2a/2b (May 2020): *meeting cancelled*; proposed **6-month delay** to original timeline.

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<td>Step 3/4 (May2022)</td>
<td>Sign-off and adoption</td>
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May 2020 (4th meeting)

**Virtual meeting** to continue development of the technical document.

Comments from EWG constituencies to be collated and distributed to EWG.

**Critical areas to be discussed** will be identified from comments.

**Continued consensus building.**

**Continue revision of guideline and annexes** over the summer.
ICH Q13 Expert Working Group
Acknowledgements

• ICH Q13 EWG
• Dolores Hernan, EMA (Deputy Topic Lead, EC/Europe)
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