LOGFILE Feature 37/2020

ICH Update Quality Initiatives

A report on the lecture by Roger Nosal, Pfizer, 2020 PDA/FDA Joint Regulatory Conference

by Sabine Paris

For almost 30 years now, the PDA/FDA Joint Regulatory Conference has been taking place once a year. From 14 to 16 September 2020 it was a virtual-only event for the first time. The title of the conference was "The Future Is Now: Effective Quality Management and Robust Manufacturing".

Roger Nosal from Pfizer is the rapporteur of the ICH Internal Quality Discussion Group (IQDG) and presented goals, achievements and guidelines that are currently being updated. The IQDG focuses on technical and scientific aspects in its work. It aims to ensure that the ICH guidelines are up-to-date and reflect the current scientific knowledge.

The ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) has 17 members and 32 observers worldwide and is celebrating its 30th anniversary this year. Experts from industry and authorities work together to eliminate differences in the technical requirements for drug development in the three major pharmaceutical markets EU, Japan and USA. A large number of uniform, recommending guidelines (ICH guidelines) covering all aspects of the quality and safety of medicines, preclinical and clinical requirements have been drawn up and implemented in the participating countries.

Objectives of the ICH

Reduce the proliferation of the many different regulatory standards

- Harmonised, clear rules based on scientific, robust principles and contemporary standards
- ICH guidelines are intended to ...
    - Describe convergence of regulatory expectations - the "what" not the "how"
    - Be implemented holistically
    - Be accepted by the authorities as definitive and complete

ICH Accomplishments

ICH has greatly improved the global harmonisation of regulatory expectations.

ICH has

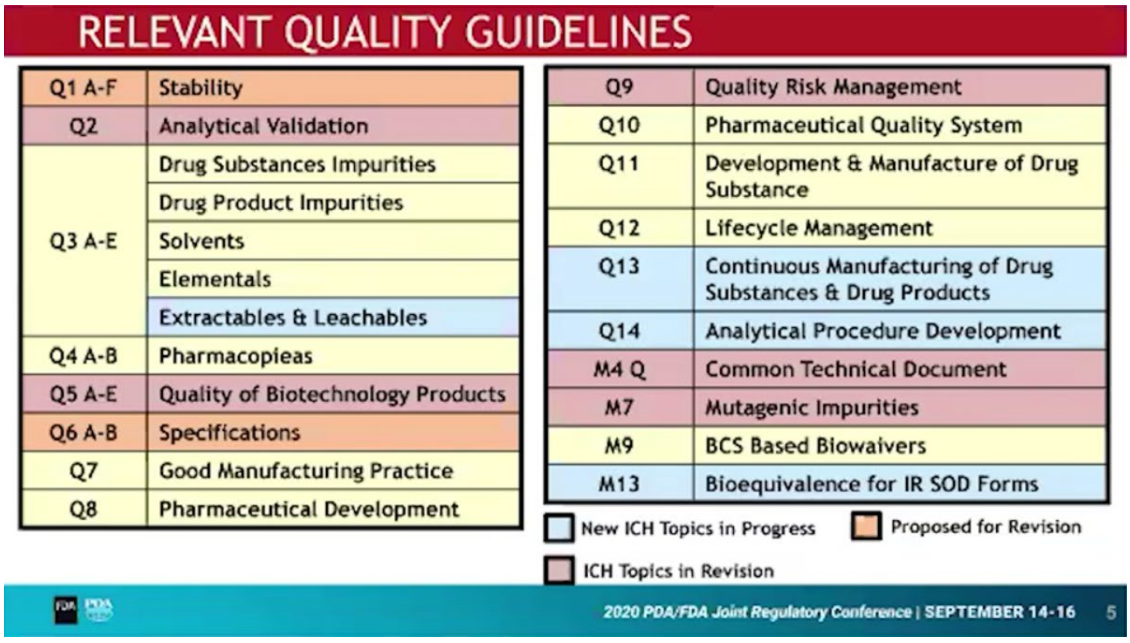
- Established common vernacular and standard conceptual definitions,
- Introduced and laveraged contemporary scientific justification and risk-based criteria,
- Improved transparency and communication between authorities and industry,
- avoided overly rigid guidelines to allow alternative approaches,
- provided meaningful examples.

Future vision for further harmonization

- Simultaneous worldwide development and filing
- Mutual recognition or joint review of marketing applications
- Pre-approval inspections follow worldwide standards (e.g. PIC/S)
- Improved post-approval change implementation
- Reduced supply chain complexity
- Reduced drug shortages
- Reduced administrative costs for pharmaceutical industry
- Increased patient access to medicines

New / to be revised Guidelines

The ICH Internal Quality Discussion Group (IQDG) has identified the following Quality Guidelines which either need to be established or revised:



Update on ICH Q13 Continuous Manufacturing of Drug Substances and Drug Products

Objectives of the new ICH Q13 Guideline are:

- Capture key technical and regulatory considerations that promote harmonization, including CGMP elements specific to CM
- Allow manufacturers to employ flexible approaches, i.e., focus on the „what", not „how" to develop, implement, or integrate CM for the manufacture of small molecules ans therapeutic proteins
- Provide sensible guidance to industry and regulatory authorities regarding regulatory expectations for the development, implementation and assessment of CM technologies used in the manufacture

It is planned that the document will pass Step 1 (consensus in the drafting ICH Working Group) and Step 2 a/b (consensus in the ICH Assembly) in November 2020, followed by a public consultation. The final guidance could then be published in May 2022.

ICH Q13 CONTINUOUS MANUFACTURING OF DS & DP

LOCATION/DATE	PROGRESS & PLANS
1st Mtg. in Charlotte Nov 2018	• Completed the concept paper and business plan • Formed the Q13 EWG
2nd Mtg. in Amsterdam Jun 2019	Completed the Q13 outline
3rd Mtg. in Singapore Nov 2019	Completed the 1st draft of the core Q13 Guideline
Virtual Mtg. May 2020	• Completed 2nd draft of Q13 Guideline & 1st draft of six Annexes • Collected comments through membership internal consultations
Jun - Jul 2020	Reviewed Comments
Nov 2020	• *Finalize technical document Step 1 sign-off & Step 2 a/b endorsement,* • *Initiate public consultation*
Nov 2021	*Review Public comments and develop Step3 draft guideline*
May 2022	*Step 3 sign-off and Step 4 adoption of final guideline*

Update on ICH Q14 Analytical Procedure Development und Q2 (R1) Analytical Validation

One topic that ICH has not yet addressed is the development of analytical methods. The new ICH Q14 guideline is intended to close this gap. At the same time, ICH Q2(R1) on the validation of analytical methods will be revised to complement modern analytical methods (e.g. NIR), to accomodate analytical performance criteria, multivariate models and Real Time Release Testing (RTRT).

The timeline is ambitious and final versions are scheduled for November 2021.

ICH Q14 ANALYTICAL DEVELOPMENT & Q2(R1) VALIDATION

LOCATION/DATE	PROGRESS & PLANS
Jun 2018	Formed the Q13 EWG
Nov 2018	Completed the concept paper & business plan
May 2019	Completed ICH Q2(R1) Outline
Nov 2019	Completed ICH Q14 Outline
Apr 2020	Separate drafts for Q2 and Q14 with unified glossary issued to membership for comments
Nov 2020	• *Finalize technical document Step 1 sign-off & Step 2 a/b endorsement,* • *Initiate public consultation*
May 2021	*Review Public comments and develop Step3 draft guideline*
Nov 2021	*Step 3 sign-off and Step 4 adoption of final guideline*

The most critical Update: ICH Q9 Quality Risk Management (QRM)

Rogar Nosal attached particular importance to the revision of ICH Q9. Risk management is now routinely applied in all areas of pharmaceutical production. Amendments to the guideline have become necessary as discrepancies have become apparent between how risk management is used in industry and how it is interpreted by the authorities.

What should ICH Q9 pay more attention to?

- High levels of subjectivity in risk assessments and in QRM outputs
- Product availability risks
- Lack of understanding as to what constitutes formatlity in QRM work
- Lack of clarity on risk-based decision-making

Training materials will also be developed to introduce the changes and facilitate their implementation.
The final concept paper, which, according to Roger Nosal, looks very reasonable, is expected to be published in November 2020. The final version of the guideline is planned for 2022.

ICH Q9 QUALITY RISK MANAGEMENT REVISION

LOCATION/DATE	PROGRESS & PLANS
Nov 2020	Final Concept Paper and Business Plan endorsed
Sep - Oct 2021	Step 2b (Adoption of the draft guideline)
Nov 2021 - Jan 2022	Step 3 (Regulatory Consultation)
Nov 2021 - May 2022	Development of Training Materials
Jun 2022	Step 4 (Adoption of final ICH Guideline and the training materials)

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