Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management: ICH Q12

Andrew Chang, Ph.D.
Vice President, Quality and Regulatory Compliance, Novo Nordisk Quality
A member of ICH Q12 EWG, representing PhRMA

4th FDA/PQRI Conference on Advancing Product Quality
Rockville, MD, 9-11 April 2019

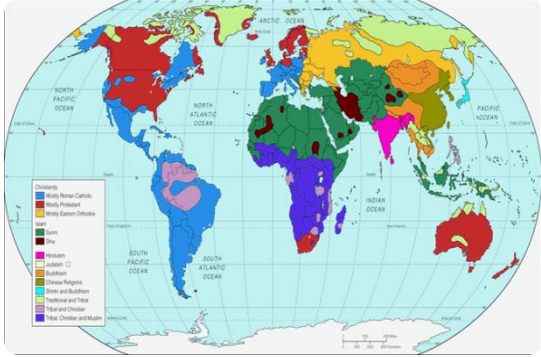
ICH Recognised Training Programme

novo nordisk®

Disclaimer

- The speaker is solely responsible for the content of this presentation
- The views presented here do not necessarily represent the views of ICH, PhRMA or Novo Nordisk

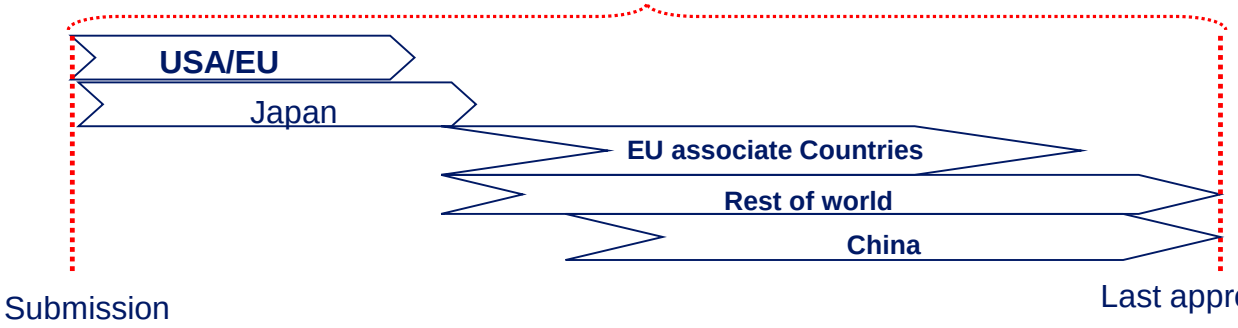
Why ICH Q12?



Diverse global regulatory environment for post-approval changes

Example of a single change: introduce a new filling site

Total expected approval lead time for a world wide approval



Result:

- For a new filling site, long and different approval time lines => some countries will have to be supplied from the old filling factory for four years.
- Company must be able to produce different variants of the same product

Why Q12?

Another industry and regulators joint effort to reaching the **Desired State**

“A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight.”

- ICH Q8, Q9, Q10 and Q11 provided much of the framework
- ICH Q12 intended to **be more operational** and cover product lifecycle management

novo nordisk®

Q12 Objectives (from the Q12 concept paper)

- …**Harmonize change management**…in a more transparent and efficient manner…across ICH regions
- …Facilitate **risk-based** regulatory **oversight**…
- Emphasize…**control strategy** as a key component of the…dossier
- Enhance use of regulatory tools for **prospective change management**…enabling **strategic** management of **post-approval changes**…

novo nordisk®

Additional Objectives

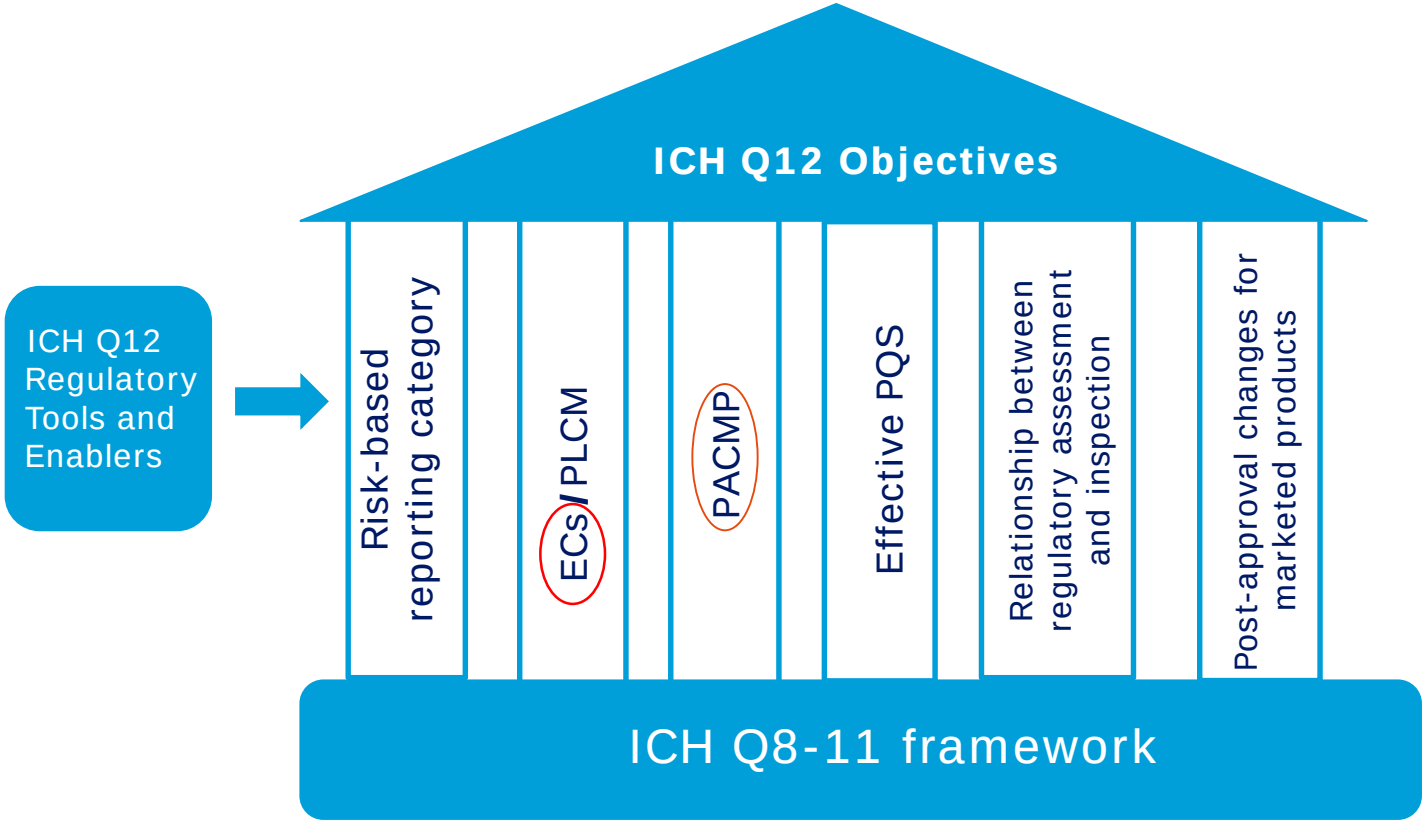
- Provides a framework to streamline the management of post-approval CMC changes in a more predictable and efficient manner
- Encourages innovation and continual improvement
- Bring envisioned operational/regulatory flexibility to fruition, e.g., by demonstrating how enhanced product and process knowledge contribute to a reduction in the number of post-approval regulatory submissions

novo nordisk®

Q12 Expert Working Group (EWG)

- Large team representing regulators (FDA, EC, MHLW/PMDA, HC, Swissmedic, ANVISA, NMPA, MFDS, HSA, WHO, TFDA) and industry (PhRMA, EfPIA, JPMA, IGBA, BIO, APIC, WSMI)
- Diverse technical, quality and regulatory expertise
- Strong leadership, and excellent collaboration and dedication
- Commitment to develop a transformational guideline
- Willingness to discuss and resolve difficult technical and regulatory issues

novo nordisk®



- Use existing effective tools
- Identify new tools
- Find the way to build trust and enhance communication
- Structured approach for frequent post-approval changes of marketed products

novo nordisk®

Table of Content

- ICH Q12 Core Document and Appendices

novo nordisk®

Table of Content

- ICH Q12 Annex (illustrative examples)

novo nordisk®

Chapter 2: Categorization of Post-Approval CMC Changes

- Considers a risk based system for categorization of changes and regulatory communications (prior approval, notification and no reporting)
- System exists in some markets
- Global implementation will allow timely and efficient introduction of CMC changes and enable effective use of industry and regulatory resources
- Lowest risk changes are only managed and documented within the PQS and not reported to regulators
  - May be verified on routine inspection

novo nordisk®

Chapter 5: Product Lifecycle Management (PLCM) Document

- Serves as a central repository of the ECs, reporting category for making changes to approved ECs, PACMPs, and post-approval CMC commitments
  - Facilitates and encourages a more strategic approach to lifecycle management
  - Enables transparency and facilitates continuous improvement

- Maintenance
  - Updated list should be submitted in post approval submissions for CMC changes
  - ECs should be updated based on knowledge gained during the lifecycle

novo nordisk®

Chapter 6: Pharmaceutical Quality System (PQS) and Change Management

- Reinforces Q10 PQS expectations to effectively implement Q12
- Discusses the essential relationship between sponsor and sites PQS's regarding EC maintenance, revision, and change management
- Emphasizes 'best practices' of change management process
- Highlights the need for active KM and QRM in driving change and maintaining ECs over the lifecycle
- Discusses inspection impact on established conditions
  - ECs may be reviewed and modified as part of remediation efforts following a violative inspection, particularly where observations indicate problems with the firm's ability to manage changes

novo nordisk®

Chapter 7: Relationship Between Regulatory Assessment and Inspection

- Regulatory assessment and inspection are complimentary activities and their role remain unchanged by Q12
- Q12 encourages communication between assessors and inspectors to facilitate implementation of Q12
- Communications between regulators across regions will proceed in accordance with appropriate bilateral and multilateral arrangements

Chapter 8: Post-Approval Changes for Marketed Products

- Q12 regulatory tools/enablers are applicable to both new and marketed products
  - In most cases, industry is less likely to invest in enhanced/QbD development of old products to define EC and utilize specific regulatory benefits
- Q12 describes a strategy for a structured approach for frequent CMC changes (e.g., analytical methods) and data requirements for CMC changes (e.g., stability)
- Without this section, Q12 will have very limited benefits to the majority of marketed products (old innovator products and generics)

novo nordisk®

Finalization of Q12: Next steps

- Public Consultation extended for one year
  - Regional review of comments Q1-4, 2018
  - ICH Q12 EWG Interim Meeting – February 11-15, Tokyo, Japan
  - Step 4 Targeted for Q2 2019 – June 2-7, Amsterdam, The Netherlands

- Training
  - Development of a comprehensive training program and supporting documentation sponsored by ICH is highly recommended to ensure the proper interpretation and effective utilization and implementation by industry and regulators
  - This is important not only for ICH, but also for non-ICH regions
  - Q12 Training subteam established and will build on Q-IWG best practices

novo nordisk®

Take Home Messages (1)

Q12 is a transformational guideline

- Introduces a harmonized risk-based categorisation system for managing post-approval CMC changes under ICH framework (Global benefits)
- Provides clarity to distinguish between ECs and supporting information in a regulatory submission
- Improves transparency on actual “regulatory commitments”, which are subject to regulatory change control
- Expected fewer PAS and Type 2 variations resulting in speedy implementation of manufacturing changes

novo nordisk®

Take Home Messages (2)

Q12 is transformational guideline

- Enables planning and implementation of future changes to ECs in an efficient and predictable manner by using PACMP

- PLCM document serves as a central repository of the ECs, reporting category for making changes to approved ECs, PACMPs, and post-approval CMC commitments

- Provides a strategy for a structured approach for frequent CMC changes (e.g., analytical methods) of marketed products

novo nordisk®

Acknowledgements

- Moheb Nasr, Former GSK, Rapporteur of Q12 EWG for step 1 Document
- Ashley Boam, FDA, Rapporteur of Q12 EWG after step 1 document
- Q12 EWG Team

Thank you for your attention