Regulatory Requirements and Case Sharing on Post Approval Change Management Protocol

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Agenda

Introduction to Post-Approval Change Management Protocols

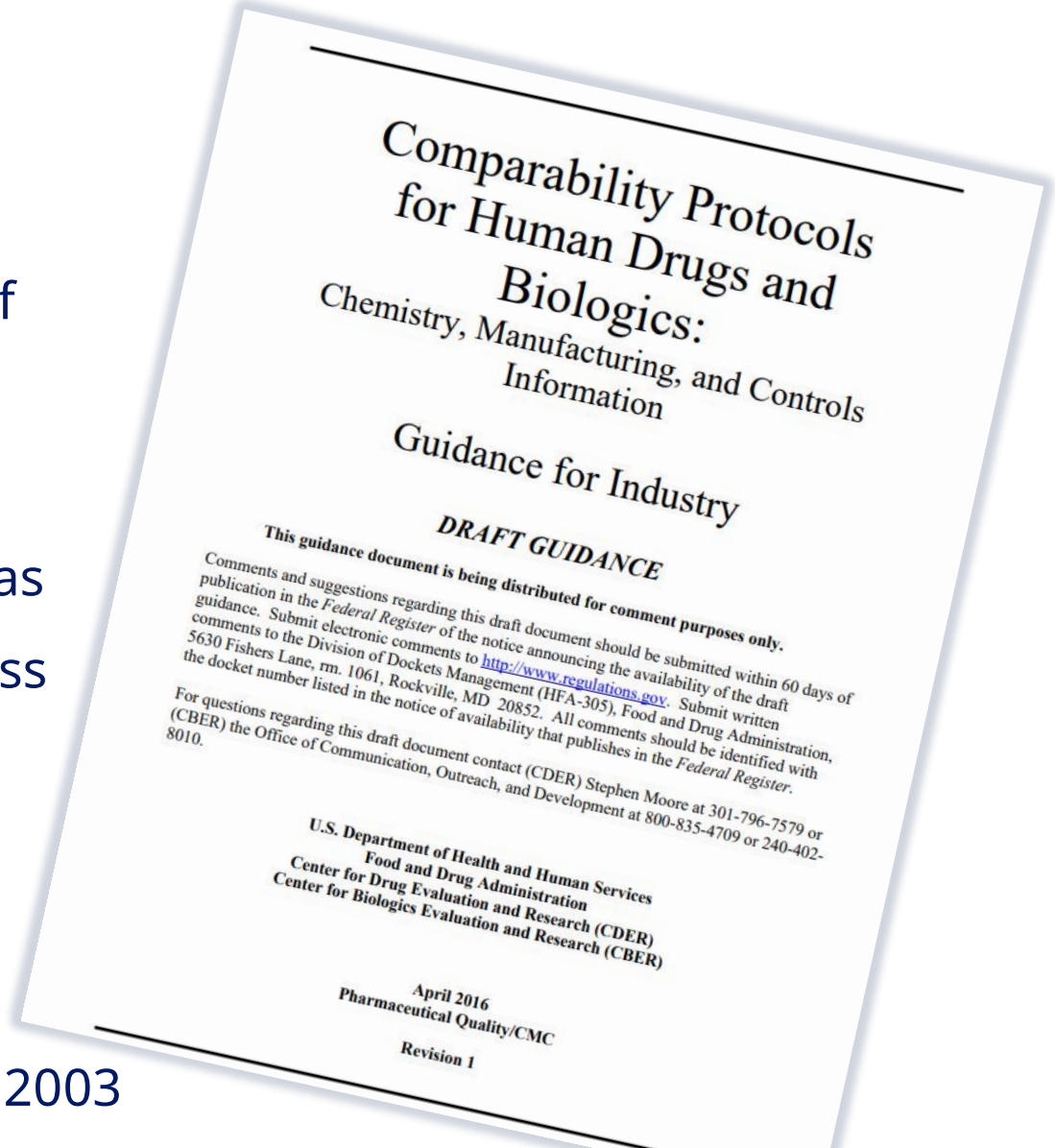
Case study (I): Additional site for an insulin product

Case Study (II): Sterile filtration at point of filling

Conclusion

FDA was first with the PACMP – termed Comparability Protocol

A Comparability Protocol is a comprehensive, prospectively written plan for assessing the effect of a proposed CMC post-approval change(s) on the identity, strength, quality, purity, and potency of a drug product or a biological product (i.e., product), as these factors may relate to the safety or effectiveness of the product (i.e., product quality).



Comparability Protocols for Human Drugs and Biologics:
Chemistry, Manufacturing, and Controls Information

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Stephen Moore at 301-796-7579 or (CBER) the Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2016
Pharmaceutical Quality/CMC

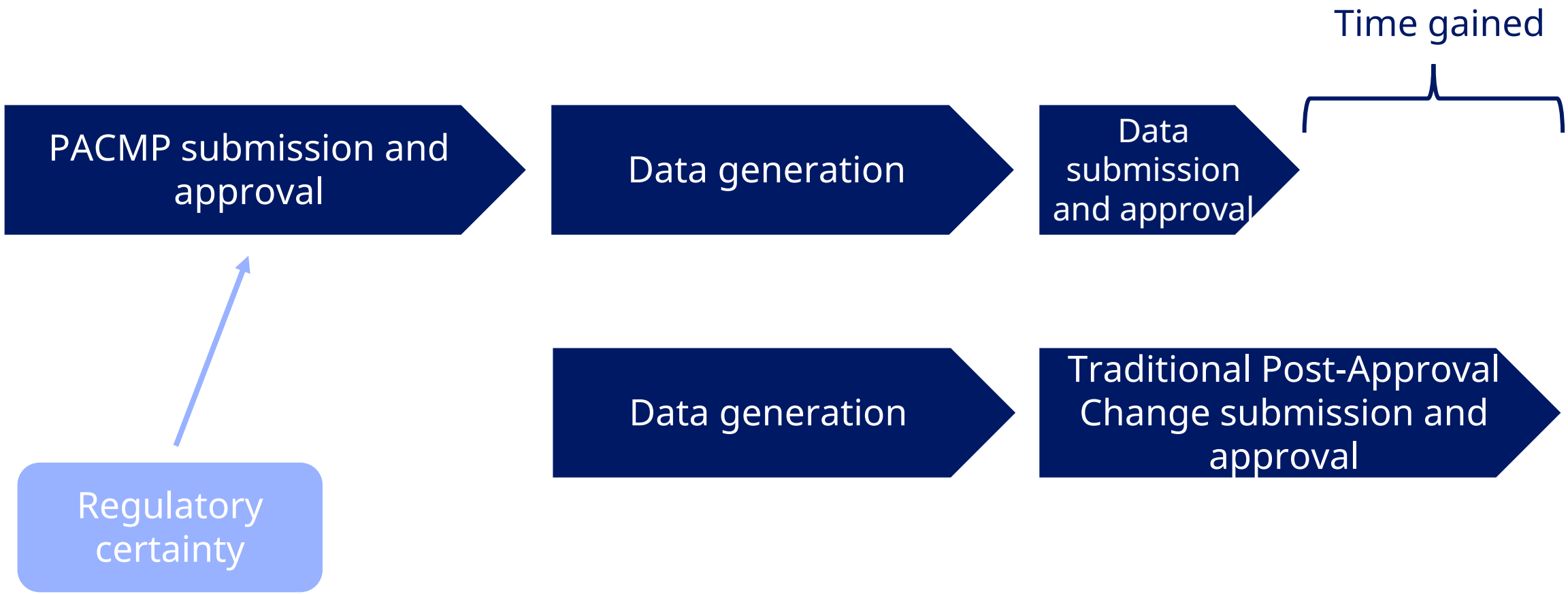
Revision 1

First version 2003

PACMPs are being introduced globally

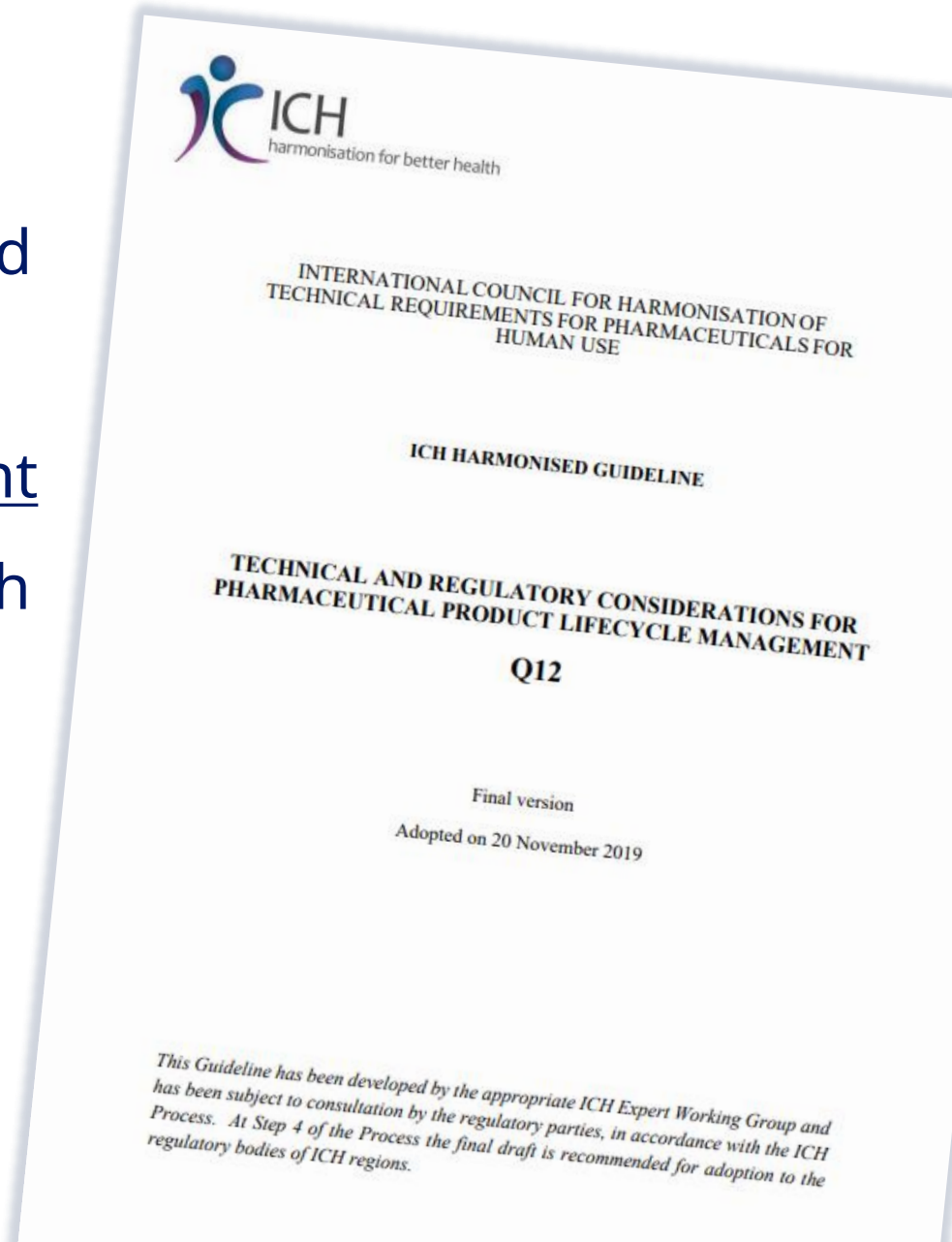
- USA introduced the PACMP (Comparability Protocol) in 2003
- EU allowed PACMP in 2013
- Switzerland is allowing PACMP from 2019
- Japan introduced the PACMP in Aug 2021
- Canada introduced PACMP under pilot in Nov 2021
- Brazil is about to commence a Q12 pilot, starting with PACMP tool

Post-Approval Change Management Protocol



ICH Q12

The PACMP is a regulatory tool that provides predictability regarding the information required to support a CMC change and the type of regulatory submission based on prior agreement between the MAH and regulatory authority. Such a mechanism enables planning and implementation of future changes to ECs in an efficient and predictable manner.



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INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

TECHNICAL AND REGULATORY CONSIDERATIONS FOR PHARMACEUTICAL PRODUCT LIFECYCLE MANAGEMENT

Q12

Final version

Adopted on 20 November 2019

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of ICH regions.

ICH Q12

A protocol describes the CMC change an MAH intends to implement during the commercial phase of a product lifecycle, how the change would be prepared and verified, including assessment of the impact of the proposed change, and the suggested reporting category in line with regional regulations and guidance, i.e., a lower reporting category and/or shortened review period as compared to similar change procedure without an approved PACMP. The PACMP also identifies specific conditions and acceptance criteria to be met.

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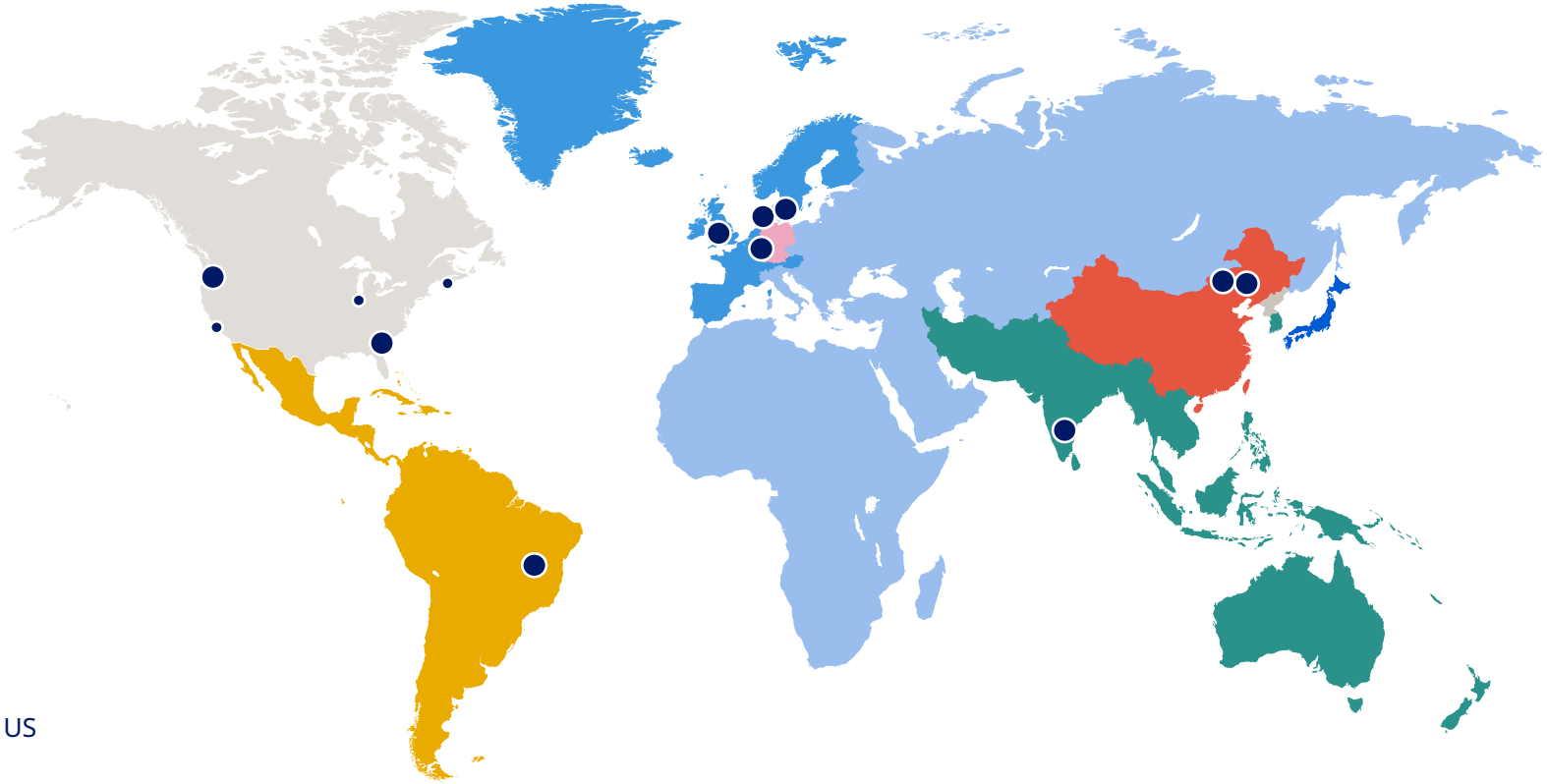
Our **global** presence



Corporate headquarters
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Strategic production sites
Brazil, China, Denmark, France, US

R&D centres
China, Denmark, India, UK, US

Regional offices
- Beijing (China)
- São Paolo (Latin America)
- Tokyo (Japan)
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- Dubai (Asia & Pacific)

168 Novo Nordisk markets its products in **168 countries** worldwide

80 Novo Nordisk affiliates in **80 countries**

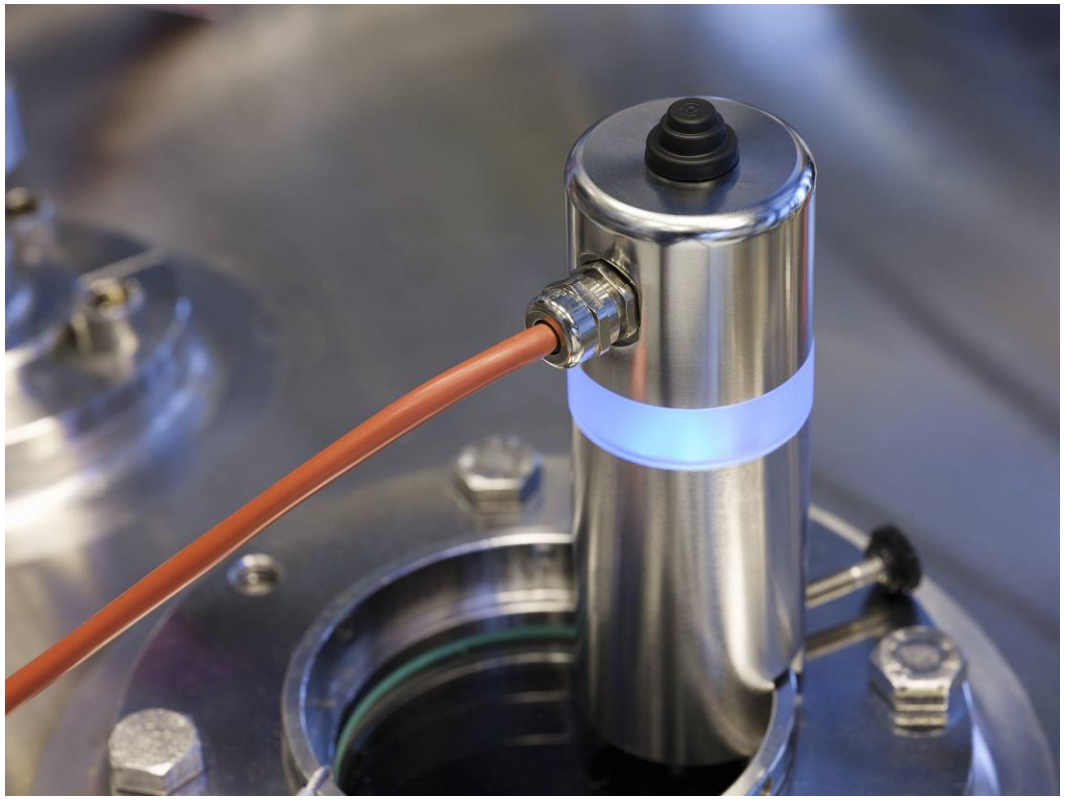
Case example (I): Additional drug product site for an insulin analogue

- The same process as original site
- Within the approved batch size range
- The same specification
- The QC lab was already approved
- The facility already had satisfactory GMP approval

- Submitted as a type II variation in EU: Post-Approval Change Management Protocol

Submission of data in a Type 1b variation

- Addition of manufacturer
- Facility and Equipment
- Process validation report
- Batch analysis report
- Stability protocol
- Change managemant report



Time line

- Type II (major change) PACMP submitted: 03-May-2019
- PACMP approved: 18-Jul-2019
- Results submitted as Type 1B (moderate change): 23-Sep-2020
- Addition site approved: 04-Nov-2020
- Batches from new site can be released from: 04-Nov-2020

Case example (II): Sterile filtration at point of filling (soluble insulin products)

- Protocol describing how pilot data for batches with and without the sterile filtration at point of filling will be made
- Acceptance criteria:
  - The results of stability indicating parameters, e.g. pH, macroscopy and preservatives must be within the currently approved release specification limits, comparable to reference samples produced without the sterile filter at point of filling and comparable to historical data in manufacturing scale.
- Submitted as a type II variation in EU: Post-Approval Change Management Protocol

Submission of data in a Type 1b variation

- Updated decribtion of manufacturing process and controls
- Batch analysis report
- Stability protocol and commitment
- Change management report

Time line

- Type II PACMP submitted: 20-Dec-2020
- **PACMP approved: 11-Mar-2021**

- Results submitted as Type 1B: pending

Conclusion

- PACMPs are very usefull for major changes for which lower reporting category of data is expected (and approved ☺)
- Major logistical advantages as time from manufacturing to release can be shortened
- Predictability of the resulting post-approval change