

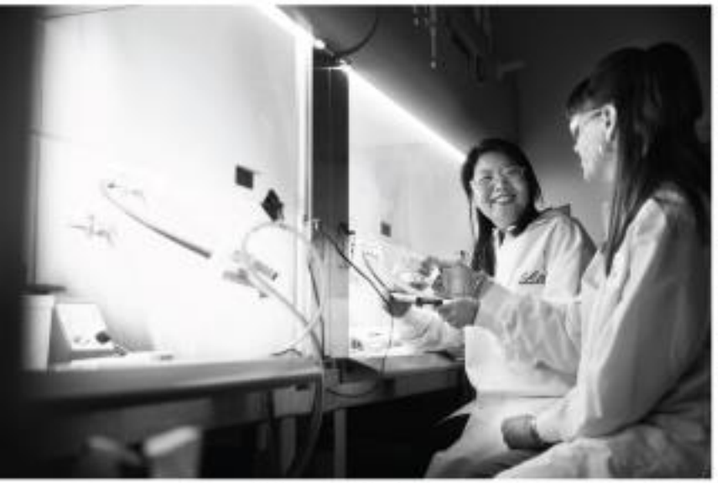


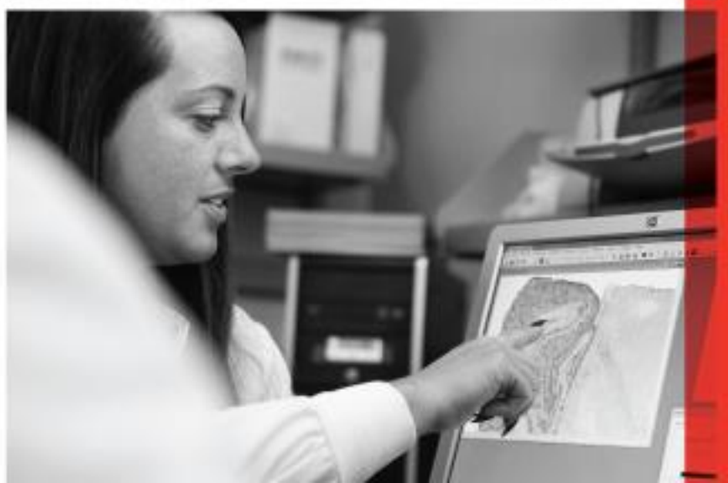

Comparability Protocols – a Love/Hate Relationship

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Agenda

- Overview of the Regulatory Pathway
- Expansion of use beyond US and EU through ICH Q12
- Things to Love
- Things that Frustrate
- Scenarios

What is a CP or CMP?

- Comparability Protocol (US) or Change Management Protocol (EU) is:
  - Prospectively written describing:
    - What will change
    - How change(s) will be assessed for impact
    - Scope of use (single or repeated use)
    - Scope of product (single drug substance/product, or many)
  - Binding Commitment

Established Pathway

- US FDA Guidance
  - 2016 Comparability Protocols for Human Drugs and Biologics: CMC Information Guidance for Industry
- EU Variation Categories
  - B.I.e.2 (drug substance)
  - B.II.g.2 (drug product)

ICH Q12

- Regulatory pathway proposed in ICH Q12 drafts (to date)
- May require local changes in regulation for some ICH members

Why “Love/Hate Relationship”?

- Advantages
  - Alignment with health authority regarding science to be presented
  - Mfg knows exactly the data set to deliver to Regulatory
  - Ability to reduce reporting category once data are available
- Frustrations
  - Loss of flexibility to respond to the unexpected
  - Lead time required
  - Customer desire to “buy-down” every PAS
  - Distinct restrictions from use in US guidance

SCENARIOS

Construction within sterile facility changing equipment/people/product flow

- Why you might choose CP
  - Gain alignment on multi-phase project
  - Ensure alignment on EM, aseptic simulation data to be provided
  - Timing, timing, timing
- Why you might not
  - Changes so drastic as to require GMP inspection (guidance precludes use)
  - Project scope creep is real!

Establishing a new manufacturing site

- Why you might choose CP
  - Gain alignment on science to be presented
- Why you might not
  - GMP inspection requirement
  - Loss of flexibility (acceptance criteria must be pre-defined)
  - Low likelihood of decreased reporting

Complex change (multiple concurrent changes)

- Why you might choose CP
  - Gain alignment on science to be presented
  - Timing, timing, timing!
- Why you might not
  - Loss of flexibility (acceptance criteria must be pre-defined)

Introduction of a new product (impacting cleanibility) to a multiproduct, biologics facility

- Why you might choose CP
  - Anticipated CBE-30/PAS scenario throughout life of product
  - Ensure consistent data package expectations
  - Timing, timing, timing!
- Why you might not
  - Loss of flexibility (acceptance criteria must be pre-defined)

Acknowledgements

- Regulatory colleagues
  - Sally Anliker
  - Khalid Mahmood
  - Juliana Stuckey
  - Isabelle Auriol
- As well as the many technical experts who have contributed to the protocols which have been successfully utilized to date!