Experience in Implementing ICH Guidelines Q1-Q7

Perspectives from Industry

Workshop on Implementation of ICH Q8/Q9/Q10 and Other Quality Guidelines

Presented by JCCT

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Presentation Outline

• The Guiding Principle for Pharmaceutical Product Development
• What’s easy and what’s not
• Impurities
• Specifications
• Submission package
• Conclusion

This presentation will give some examples to illustrate the experiences in implement the ICH guidelines for selected topics.
Guiding Principle

- Pharmaceutical products must have the highest possible quality and effectiveness
- ICH guidelines provide a common set of standards to guide the product development and evaluation
- ICH guideline will work well only with the correct frame of mind – self discipline is a must
- Work with the regulatory agencies early on
What’s Easy and What’s Not in Implementation

• Easy
  – To understand the guidelines
  – To follow what is written in the guidelines

• Not easy
  – To interpret what is implied
  – To expect “it covers all”
  – To “go around”
Impurities in Drug Substance and Drug Product

• Drug substance
  – Impurity profile must be very well studied
    • Innovator
    • Generic
    • Establish adequate test methods and specifications
  – Understand the mechanism for the change of potency
    • Is the mass balanced?
    • Why the increase of potency?
  – Understand the implications to the drug product
    • Interactions with excipients and/or packaging materials
    • Change in polymorphic forms
Impurities in Drug Substance and Drug Product

• Drug product
  – Degradation of API in drug product during storage
  – Impurities arising from excipients
  – Impurities arising from container closure system
Impurities in Drug Substance and Drug Product

• An example

  – Drug A:
    • 1g in 10 ml for pain control
    • Patient can self administer the drug by pushing a button to get 1 ml of the drug through existing IV line
    • As frequent as once every hour
  – In theory:
    • Maximum daily dose = 1g/10ml x 1ml/hour x 24 hours/day = 2.4 g/day
  – ICH guideline:
    • MDD >2g/day, quantification threshold 0.05%
    • MDD ≤2g/day, quantification threshold 0.15% or 1.0 mg per day intake (whichever is lower)
  – In reality:
    • Patient is very unlikely to self administer every hour in 24 hours.
    • Make the qualification of impurities unnecessarily more difficult
    • Need better communication with the agencies
    • Need better labelling of the drug
Specifications

• Set realistic specifications for potency
  – Specification is driven by the clinical requirement
  – Test method has to be able to support the specification
  – In process vs. release specification
    • In process spec to make sure the process is carried out correctly
    • Release spec to make sure product quality
    • Same method can be used – pros and cons

• Residual solvent spec to match manufacturing capability
  • FDA deficiency letter for class III solvent
Submission Package

• Use the CTD template to begin with
  – QbR is designed to guide you to do a good job in QbD
  – Very easy to use
  – Very easy to make a mistake

• Submission package review to ensure quality
  – Technical review
  – Peer review
  – Management review
Conclusion

• ICH guidelines are guidelines

• Know your product

• Know the science behind your product

• Work with the regulatory agencies

• Quality is a frame of mind
  – form the correct frame of mind throughout the organization
Thank You