EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Quality aspects in IMP developments

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Structure

- Importance of relevant Quality information in a CT application
- Phase-dependent requirements for Quality documentation
- EU guideline on Quality requirements of IMPs + Q&As
- Relevance of keeping a future MA application in mind
- Examples

Include relevant Quality information in CT applications

- Quality documentation (CMC)
- Equally important as other parts of submission
- Basis for drawing conclusions from the CT and links to future MA application
- Avoid major objections to the CT documentation during assessment

Phase-dependent requirements for Quality documentation

Focus on risk aspects:

- Nature of product
- State of development/clinical phase
- Patient population
- Nature/severity of the illness
- Type and duration of clinical trial

Same type of documentation as for MA applications, less detailed

EU GL on Quality requirements of IMPs + Q&As

Requirements to the Chemical and Pharmaceutical Quality documentation concerning IMPs in CTs

http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500003484

Q&A on Quality: Specific types of product - Quality of IMPs

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000072.jsp&mid=WC0b01ac058002c2b0#section9

(e.g. How to set specifications for impurities)

The GL and Q&As are available from the EMA Web page

EU GL (continued)

Requirements for:

- IMPs
- Modified authorised comparator products
- Placebo

In all these cases there is a requirement for GMP manufacture

EU GL (continued)

The GL is of an illustrative nature

- Not exhaustive requirements for diversity of relevant products

- With increasing complexity of product, increased level of detail in documentation would be relevant
- Sterilisation procedures other than terminal sterilisation: sufficient information on manufacturing process/validation

Keeping a future MA application in mind

- Qualification of impurities
  Level of impurities decreases with development of the synthesis
  Degradants occuring after reconstitution, if relevant
  If route of synthesis is changed, other impurities may occur
- APIs where composition or properties may vary
  Batches for commercial product must be similar to batches in CT
- At CT: Specification limits may not have been set, but important to monitor all relevant parameters
- At MAA: Differences between clinical vs commercial product assessed (formulation/composition and manufacturing process)

Examples – level of detail in different phases

- Specifications for impurities

  Phase I: tentative upper limits

  Phase II and III: adjusted to the state of development

- Validation of analytical procedures

  Phase I: Confirmation of suitability + Summary of acceptance criteria and parameters to be validated

  Phase II and III: Validation results for all relevant parameters

- Stability of product

  Phase I: Start and commitment + Justification of shelf life

  Phase II and III: In addition, results accelerated/long term conditions

Examples – keeping future MAA in mind

- Quality parameters with potential clinical relevance
- For tablets (including modified release formulations) there is no requirement to set a limit for dissolution rate. However, this should be monitored with a relevant test.
- If a polymer is used as drug substance it is important to monitor relevant characteristics such as molecular weight distribution in sufficient detail in clinical batches

Examples – important to include

- Include relevant parameters that may change during storage in stability testing (also including appearance and degradation products individually)
- Justification of specifications for impurities/degradation products
- Information/results from validation of analytical methods
- Information on description/validation for sterilisation by filtration
- Information in relation to any dilution of product before use

Thank you for your attention!