EU Biosimilar Guidelines

5th EGA Symposium on biosimilars

May 2007

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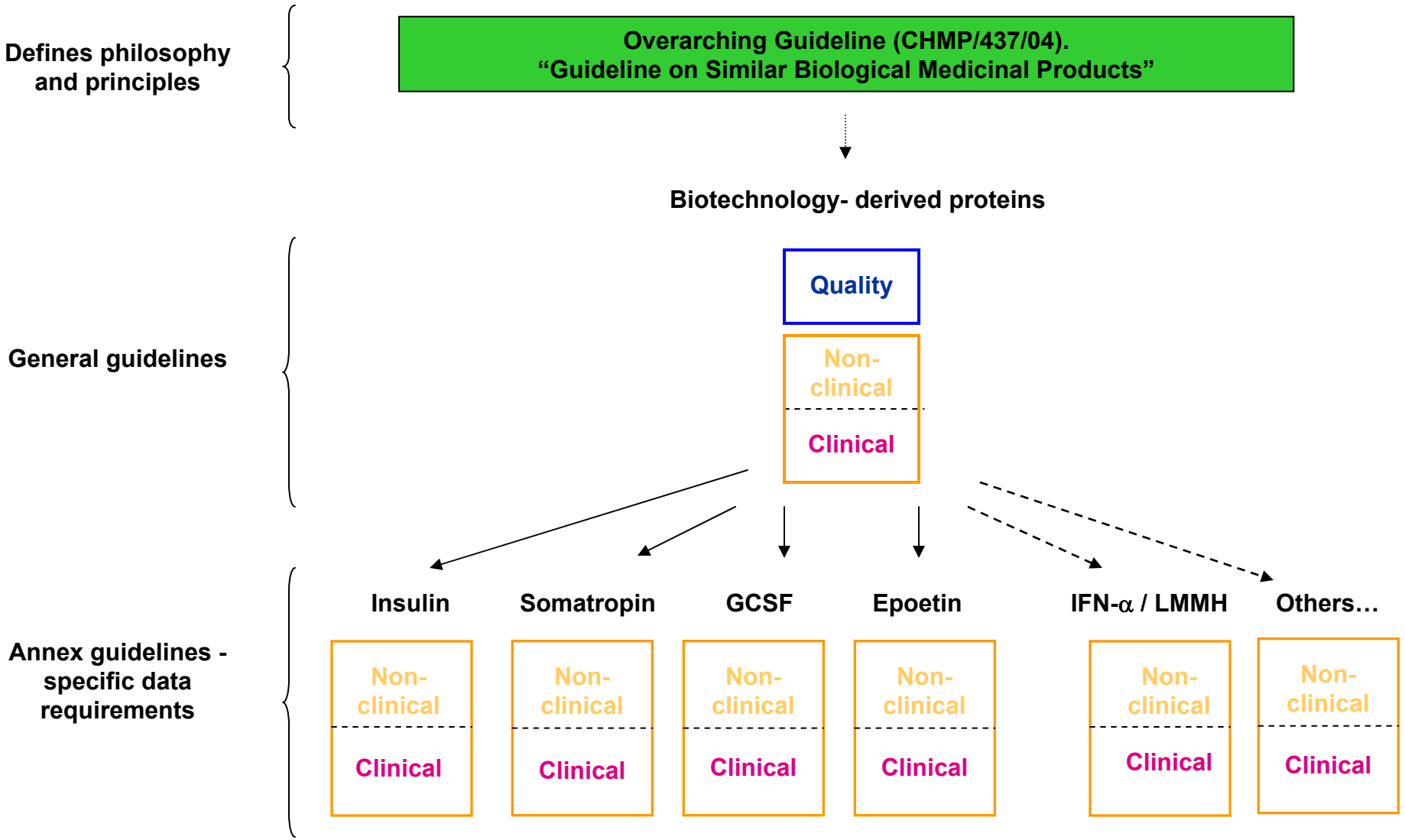
Current Biosimilar Guidelines – Summary



Current Guidelines – amendment ?

- **Experience being gained**
- **Most discussion on epoetin**
  - » Guideline did not address Contra-indication for S/C route for epoetin alfa
  - » Discussion on whether i/v alone can be authorised (risk of off-label s/c use)
  - » Potency assay range (80-125%) puts additional demands on equivalence margins
- **Amendment could be considered in medium term**

Guidelines in development

- LMMHs
- Interferon alfa
- Immunogenicity
- Comparability

Guidelines in development

- **LMMHs**
  - » Similar biological medicinal products containing low molecular weight heparins – (Non-)Clinical Issues. CHMP/BMWP/496268/06
  - » CONCEPT PAPER released for consultation Jan 2007. Comments by 30 Apr 2007
  - » Draft Guideline: release for consultation expected 4Q 2007.

Low Molecular Mass Heparin

- **Concept Paper**
  - » LMMH fits definition of biological = biosimilar route is appropriate
  - » Characterisation of complex molecules
  - » Pharmacokinetic bioequivalence not sufficient

Guidelines in development

- **Interferon alfa**
  - » Concept Paper Adopted (consultation concluded August 2006).
  - » Draft Guideline: release for consultation expected 4Q 2007.

Interferon alfa

- **Guideline Drafting Ongoing**

  - Non-clinical: Pharmacodynamics / Toxicology
  - Clinical:
    - PK / PD (any validated markers)
    - Efficacy: most sensitive population (Hep C)
    - Study design / Endpoint / Duration
    - Extrapolation of data / Indications
    - Safety: AE profile / Immunogenicity
  - Pharmacovigilance: normal requirements

Guidelines in development

- **Immunogenicity**
  - » Immunogenicity Assessment of Biotechnology-derived Therapeutic Proteins. CHMP/BMWP/14327/06
  - » GUIDELINE released for consultation Jan 2007
  - » Comments by 31 July 2007
  - » Workshop (Regulators), September 2007.

Immunogenicity

- **Guideline applicable to peptides & proteins**
  - i.e. innovator and biosimilar medicinal products

  - Risk factors
  - Predicitivity of non-clinical models
  - Assay development
  - Clinical consequences
  - Clinical safety
  - Risk management plan

Comparability / Biosimilar Guideline - Revision

(Current) situation

CPMP/3097/02 - (Non)clinical issues

SPLIT

(Future) situation

Biosimilar (non)clinical Guideline (42832)

↕

Comparability Exercise versus Reference Product

Process Changes (..BMWP/101695/06)

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Comparability Exercise following, e.g. process change (compare product before v after)

Guidelines in development

- **Comparability**
  - » Comparability of Biotechnology-Derived Medicinal Products after a change in the Manufacturing Process - Non-Clinical and Clinical.

    CHMP/BMWP/101695/06

  - » GUIDELINE released for consultation Jan 2007

  - » Comments by 30 Apr 2007

Comparability – changes to process, (Non-)clinical requirements

- **Guideline similar to ICH Q5E**
  - » Risk based approach
  - » Sequential: start with quality data
  - » Depending on risk / complexity / experience may need to perform additional (non)clinical studies.

Patient Information

- **Questions and answers**
  - **What is a biological medicine?**
  - **What is a biosimilar medicine?**
  - **How is a biosimilar medicine authorised?**
  - **How is a biosimilar medicine evaluated?**
  - **Is the safety of biosimilar medicines monitored?**

- **Summary of product characteristics**
  - Guideline may consider biosimilars (2008)

Thank you for your attention !

- **For your information:**
  - » EMEA Website: http://www.emea.europa.eu
  - » Biosimilars:
    http://www.emea.europa.eu/htms/human/humanguidelines/multidiscipline.htm
  - » Peter.Richardson@emea.europa.eu