

# Regulation of Similar Biological Medicinal Products in the EU

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# Overview of the Regulatory System

- Approval systems
  - National
  - Mutual recognition and decentralized procedures
  - Centralized procedure
- Centralized system mandatory for new biotechnology products
  - Key institutions:
    - European Medicines Agency (EMA)
    - Committee for Medicinal Products for Human Use (CHMP)

# Less-than-Full Applications

- Abridged (generic)
- Bibliographic
- Hybrid
- None deemed appropriate for most biological products
  - No assurance that active principles are the “same”
  - No assurance that published literature is relevant to follow-on product

# New System for Similar Biological Medicinal Products

- Legislative elements
  - Amendment to Annex I of Directive 2001/83/EC
    - Effective October 2003
  - Article 10.4 of Directive 2001/83/EC
    - Effective October 2005

# Annex I

- Biological substance definition
  - Broadly worded to encompass all biological substances for which physical-chemical testing may be insufficient
- Generic approach not ordinarily appropriate
- Specific data governed by detailed guidance

# Article 10.4

- Ratifies Annex I
- Expressly refers to Annex I and guidance

# CHMP Guidance Process

- Role of working parties and national authorities
- Concept papers and draft guidance
- Opportunities for comment

# Principal Guidance Documents

- Similar biological medicinal products
- Biotechnology-derived proteins
- Immunogenicity
- Product-specific guidance
  - Erythropoietin
  - G-CSF
  - Human insulin
  - Somatropin
  - $\alpha$ -interferon
  - Low molecular weight heparins

# Approval Decisions to Date

- Two somatropin products approved
  - Omnitrope (reference: Genotropin)
  - Valtropin (reference: Humatrope)
- One  $\alpha$ -interferon product refused
  - Alpheon (reference: Roferon)

# Key Features of System

- Substantial period of data exclusivity
  - 10 years for pre-2005 reference products
  - 8+2+1 for post-2005 reference products
- No link to patent system
- Substantial data requirements
  - Extensive preclinical data
  - Clinical data required in all cases to date
  - Special emphasis on immunogenicity
  - Post-marketing requirements
- Products treated as “similar” rather than generics
  - Substitution decisions made by Member States
  - But CHMP guidance suggests that biosimilars are not generic equivalents