

Biosimilars: Where Are We Now?

Richard Kingham
Covington & Burling LLP
London and Washington, DC

COVINGTON & BURLING LLP BRUSSELS LONDON NEW YORK SAN FRANCISCO WASHINGTON

Topics

- Regulatory situation in the EU
- U.S. and other jurisdictions
- Key issues to be addressed in U.S.

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European Union

- EU recognized that generic procedures were inappropriate for biosimilars
 - True generic approval procedure inappropriate, because there was no guarantee that active ingredients were the “same”
 - Bibliographic procedure inappropriate, because there was no assurance that scientific literature relating to reference products was relevant to biosimilar product

European Union

- New system was established
- Similar biological medicinal products
 - Not generic approvals
 - Bioequivalence not sufficient
 - Additional tests and studies required
- Legislation contemplates issuance of detailed guidelines by Committee for Medicinal Products for Human Use (CHMP)
- To date, substantial nonclinical and clinical data have been required
- Marketing authorization applications are submitted to European Medicines Agency (EMA) and reviewed by CHMP

Guidance Process

- CHMP issues guidance
 - General
 - Product-specific
- Usual process includes
 - Concept paper for comment
 - Draft guidance for comment
 - Final guidance
 - Process take about a year

Guidelines

- CHMP has issued
 - General guidance on biosimilars
 - Guidance on biotechnology-derived proteins
 - Guidance on immunogenicity testing
 - Product-specific guidance
 - Somatropin (hGH)
 - Human insulin
 - Erythropoietin
 - G-CSF (filgrastim)
 - Alfa-interferon (draft)
 - Low-molecular weight heparin (draft)

Applications Acted On To Date

- Approved
 - Sompatropin (reference products Genotropin and Humatrope)
 - Epoetin alfa and zeta (reference product Eprex)
 - Filgrastim (reference product Neupogen)
- Not approved
 - Alfa interferon (reference product Roferon)
 - Human insulin

Data Requirements

- Guidance issued to date contemplates significant nonclinical and clinical data
 - Characterisation
 - Toxicology
 - Nonclinical PK/PD
 - Clinical PK/PD
 - In most cases, comparative effectiveness trials and substantial clinical safety data
 - Special concern with immunogenicity

Recent Developments Outside the EU

- Canada
 - Draft guidance
 - Approval in absence of Canadian reference product
- WHO
 - Preliminary draft guidance
 - “Stand-alone” versus “biosimilar” applications

United States

- Pending bills
 - Waxman-Clinton-Schumer
 - Eshoo
 - Others
- Senate HELP Committee bill
- House Energy and Commerce Committee questionnaire

Key Issues in the U.S.

- Regulatory pathway
- Data exclusivity
- Patent litigation system

Regulatory Pathway

- Scope
- Procedure for establishing data requirements
- Extent of clinical data required
- Immunogenicity testing
- Extrapolation
- Interchangeability
- Post-marketing surveillance
- Nonproprietary names

Data Exclusivity

- Basic exclusivity period
 - Hatch-Waxman model
 - EU model
 - Senate HELP Committee model
- New indications
- Second-generation products

Patent Litigation System

- Linkage to approval process
- Litigating validity and infringement issues before exclusivity period expires
- Avoiding interference with substantive rights of patent holders
- Effect on third parties