

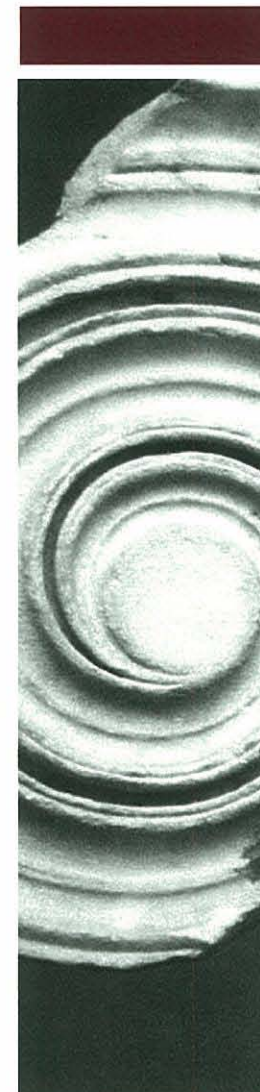
The European Experience With Follow-on Biologics Legislation

Federal Trade Commission Roundtable on
Follow-on Biologic Drugs: Framework for
Competition and Continued Innovation

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The topics I have been asked to address:

- European experience with the legislation
- European approach to exclusivity
- Exclusivity for new indications
- Exclusivity for product improvements and second-generation products
- How interchangeability is handled

The views presented are mine, not those of Hogan & Hartson LLP or any of our clients.

Similarities and Differences: EU / U.S.

Relevant similarities

- All biotech products, including biosimilars, go through centralized EMEA process (national Member State agencies might approve non-biotech biosimilars if the reference product was not one assessed by the EMEA)
- Rigorous review; much harmonization (ICH) and cooperation
- 20 years patent life; belief in strong IP system and in regulatory exclusivity

Relevant differences and a few cautionary notes

- Each of the 27 EU Member States has its own healthcare system and makes its own decisions about reimbursement, pricing etc., and medicine substitutability
- In the EU, national differences persist in the patent system.
- No linkage, no Orange Book, no Paragraph IV, no 180-day generic exclusivity in the EU: EU pharma regulators ignore patents and patent litigation
- Origin of EU 10-year exclusivity was 1987 “EU Hatch Waxman” law; biosimilar approval pathway came separately and much later (2004). In the U.S. we have the benefit of studies that might more accurately predict timelines/cost for biologics

“8+2+1”

- 8 years data exclusivity dating from the European Commission authorization decision: before that, no generic applications are fileable
- +2 years marketing protection: no generic applications approvable
- + 1 year: new indication(s) if it constitutes a significant clinical benefit
- For all products, regardless of centralized or Member State agency approval procedure
- Not retroactive; does not affect exclusivity periods for products for which applications were submitted before effective date (late 2005)

Legal provisions on improvements

- All biotech biologicals, including biosimilars, go through the centralized EMEA route. Therefore the exclusivity provision for centralized products is relevant.
- Art. 14.11 of the EMEA Regulation:
- Without prejudice to intellectual property law, **medicinal products authorized under the EMEA Regulation “shall benefit from an eight-year period of data protection and a ten-year period of marketing protection, in which connection the latter period shall be extended to a maximum of 11 years** if, during the first 8 of the 10 years, the marketing authorization holder obtains an authorization of one or more new therapeutic indications which are held to bring a significant clinical benefit in comparison with existing therapies.
- It would appear that every medicinal product that enters the EU market via the EMEA centralized procedure should receive a full 8+2+1 period. On the face of this provision, any medicinal product authorized under the EMEA Regulation “shall” be eligible for 8+2+1.

Applicants wishing to market their own versions of biotech biologics already on the market could, by submitting full applications, enjoy the benefits of Article 14.11.

This does not appear to be possible for applicants that use the biosimilar route.

“Global marketing authorization”

- There is debate as to whether a legal construct—“global marketing authorization”—in the 2004 amendment to the Community Code on Medicinal Products (new Article 6(1)) will apply to biosimilars authorized through the centralized EMEA process.
- “When a **medicinal product** has been granted an initial marketing authorization..., any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorization ...or be included in the initial marketing authorization. All these marketing authorizations shall be considered as belonging to the same global marketing authorization, in particular for the purpose of the application of Article 10(1).
- Note: European Commission guidance states that applications from different marketing authorization holders are not treated as being under the same global marketing authorization.

* Article 10(1) is the generics provision that includes the 8+2+1 provision. Article 6.1 was intended to codify case law that arose from generic applications under the previous EU pharma laws (Generics case).

“Global marketing authorization”

- The term “a medicinal product” in the provision on “global marketing authorization” is a key term.
- Changes that are treated as “line extensions” of the origination authorization (other than the indication +1) do not entitle the marketing authorization holder to get a new exclusivity period.
- However, where a 2nd generation product is a different product—e.g., a pegylated version of an older biotech product—the EMEA has treated these products as distinctive products and thus not the same “medicinal product.” Therefore, the concept of “global marketing authorization” should not stand in the way of a new exclusivity period for the 2nd product.
- However, it should be noted that there is uncertainty on this point due to case law interpreting the 1987 Directive (Novartis case).

Guidance on 11th year in 8+2+1

- It is too soon for experience with this provision.
- However, the European Commission has issued guidance, Nov. 2007, applies to both centrally authorized products and products authorized by Member States
- Guidance takes a broad view of significant benefit:
- New target disease, different stages or severity of disease, extended population for same disease
- Change from 1st line to 2nd line treatment or vice versa or from combination therapy to monotherapy
- Change from treatment to prevention or vice versa
- Change from short-term to maintenance treatment
- Improved safety, efficacy, contribution to patient care
- Applicant must justify 11th year, address existing therapy

Interchangeability - EMEA View

- *“It is not possible we would guarantee a biosimilar is interchangeable (with its originator). Substitution is a national competency and needs to be discussed at the national level”*

EMA Executive Director Thomas Lönngren, 21 July 2006

- EMEA/74562/2006, 19 April 2007

“Since biosimilar and biological reference medicines are similar but not identical, the decision to treat a patient with a reference or a biosimilar medicine should be taken following the opinion of a qualified healthcare professional.”

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