
DETAILED OUTLINE OF THE PROMOTING INNOVATIONS AND ACCESS TO LIFE-SAVING MEDICINE ACT

I. Purpose

The Promoting Innovation and Access to Life-Saving Medicine Act amends the Public Health Service Act to provide for the licensing of biosimilar and biogeneric (interchangeable) biological products.

II. Definitions

- A. Product is defined as a “biosimilar” if no clinically meaningful differences between the biological product and the original product are expected in terms of the safety, purity, and potency (safety and effectiveness) of the product.
- B. Product is “interchangeable” if it is a biosimilar and the risk of switching the patient one or more times between the original product and the biological product can be expected to be not significantly greater, in terms of safety or diminished effectiveness, than the risk of continuing to use the original product without such switching.

III. Regulation of Biosimilars and Biogenerics

A. *Submission of Abbreviated Biological Product Applications.*

- 1. Contents of abbreviated applications.
 - a. An abbreviated application for a biosimilar must demonstrate to the FDA that, among other things:
 - The product is highly similar in structure to the original product;
 - No clinically meaningful differences between the products are expected;
 - The two products have the same mechanism of action, if known;
 - The proposed product label carries one or more of the approved indications for the original product;
 - The route of administration, dosage form, and strength, are the same as the original product; and
 - The controls used in manufacturing the product are adequate to assure identity, strength, quality, and purity.
 - b. An abbreviated application for a biogeneric or interchangeable product must demonstrate to the FDA that:
 - The product is biosimilar to the original product; and

- Patients can be switched from the original product to the biogeneric without increased risk of side effects, including immunogenicity, or diminished effectiveness.
2. **Study requirements.** FDA has full scientific discretion to determine what studies are necessary to establish that (a) a biosimilar is as safe and effective as the original product, or (b) a biogeneric is interchangeable with the original product. FDA can require the applicant to conduct clinical studies in both instances.
 3. **Modified products.** The bill (like comparable provisions of Waxman-Hatch) permits submission of an application for a product that differs from, or incorporates a change to, the original product, e.g, a new dosage form, or new indication, if the application contains sufficient information to show that the new product is safe, pure, and potent (safe and effective).

B. FDA Review of Abbreviated Biological Product Applications

1. The bill requires FDA to approve an application for a biosimilar unless FDA finds (among other things) that:
 - There is insufficient information to show that the product is biosimilar to the original product, as defined in the bill, for the condition(s) of use in the proposed labeling;
 - There is insufficient information to show that product and original product have highly similar molecular structures;
 - There is insufficient information to show that the two products have the same mechanism(s) of action, if known;
 - The new product differs from the original product in route of administration, dosage form, or strength;
 - The inactive ingredients used in, or the composition of, the new product are unsafe; and
 - The controls used in manufacturing the product are inadequate to assure identity, strength, quality, and purity.
2. FDA may approve a modified version of an original product if the application contains sufficient information to establish safety and efficacy.

C. Interchangeability Determinations, Labeling, and Exclusivity. Interchangeable biological products (those that could safely be substituted for the brand name product at the pharmacy, state law permitted) would generate the greatest cost savings, but would be significantly more costly and difficult to produce than biosimilar products. The bill therefore provides incentives for the development of interchangeable products, but does not require that each biosimilar be interchangeable.

1. The bill allows an applicant for a biosimilar to request an interchangeability determination from FDA.

2. If FDA determines that a biosimilar is interchangeable with the original product, the bill permits the label of the product to state that the product is interchangeable with the original product for the approved conditions of use.
3. For each approved biosimilar, FDA must publish a determination either that the product is interchangeable for one or more specified indications, or that interchangeability has not been established.
4. If an applicant is the first to establish that its product is interchangeable with the brand name product, the bill prevents FDA from approving a subsequent application for an interchangeable version of the original drug, until the earlier of (a) 180 days from first commercial marketing; (b) 1 year after a final court decision or dismissal with prejudice of all patent infringement cases instituted under this subsection; (c) 36 months after approval if such patent litigation is ongoing; or (d) 1 year after approval, if no such patent litigation was instituted. The bill also prohibits the marketing of a “rebranded interchangeable product” distributed with the authorization of the original product holder during the exclusive marketing period.

D. Final Action on Applications

1. FDA must approve or disapprove an application for a comparable biological product ten months after submission, or 180 days after the application is accepted for filing by FDA, whichever is earlier, unless the final action date is extended by joint agreement of the applicant and FDA.
2. The bill contains provisions to prevent frivolous petitions from delaying the approval of biosimilars and biogenerics. FDA must not fail or refuse to take action by the final action date on the ground that a third party has made such a request, nor may a court enjoin FDA from taking final action or staying an approval except by permanent injunction. A permanent injunction may not be issued unless the person seeking the injunction demonstrates an injury of more than irrecoverable economic loss. A company may not file a lawsuit concerning a late-filed petition until 180 days after it was filed.

E. Postmarket Safety Studies

FDA is authorized to require post-market safety studies for biosimilar products to the same extent that such studies can be required for original products.

F. Exclusivity

1. ***Original exclusivity.*** The bill grants original biological products the same exclusivity periods (periods without generic competition) that currently are available under Hatch-Waxman for traditional drugs. Original biological

products, as defined in the bill (see “evergreening issues” below), would get 5 years of exclusivity and certain modifications of existing products would get 3 years.

2. ***Extensions of exclusivity.*** The bill provides for extensions of the 3 and 5 year periods by up to 1 year:
 - a. Provides a 3-6 month extension of the initial exclusivity period, if the original applicant obtains approval of a medically important new use of the product no later than 1 year before the original period of exclusivity expires. The extension is for 6 months, unless the product has U.S. sales of more than \$1 billion per year, in which case the extension is for 3 months.
 - b. Provides 6 months of pediatric exclusivity for conducting pediatric studies of biologics, if exclusivity is awarded more than 9 months before expiration of existing exclusivity or patent protection.
3. ***Evergreening issues.*** To prevent companies from making minor structural changes to their products to gain sequential periods of exclusivity on essentially the same product, the 5-year exclusivity provision in Waxman-Hatch was limited to “new chemical entities”: innovative drugs identified by their novel molecular structures. This bill limits the 5-year period to an analogous set of biologics: those that are sufficiently different from other approved biologics in molecular structure to require a full new application, i.e., no reliance on any of the clinical studies in any other application. The bill also specifies certain types of minor changes in molecular structure that will not be eligible for 5 years of exclusivity (though they may be eligible for 3 years). The list is drawn from a current FDA regulation defining orphan drug exclusivity for large molecules (21 CFR 316.3(b)(13)).

The 3-year period under Waxman-Hatch was limited to product modifications significant enough to require the applicant to conduct a new clinical study. Because one or more clinical studies will frequently be required even for biosimilars (products with no intended differences), the 3-year period for biologics is limited to products that both require new clinical studies and represent a “significant therapeutic advance.”

G. *Patents.* Prompt resolution of patent disputes helps ensure that irrelevant or invalid patents do not delay competition in the marketplace. Provisions in Waxman-Hatch to ensure early resolution of patent disputes have not always worked as intended. This bill adds new disincentives for late patent suits, by limiting patent infringement actions and remedies in appropriate cases.

1. ***Patent Requests.*** Biosimilar applicants may elect to ask the holder of the original product for a list of patents related to the product. The holder must respond within 60 days with a list of all related patents, including process patents, owned

by or licensed to the holder. For a period of 2 years, the holder must update the list within 30 days of the issuance a new related patent or license.

2. ***Patent Notifications.*** The biosimilar applicant may elect to notify the original product holder and patent owner that it intends to challenge one or more patents from the list provided. Any notice must contain a detailed statement of the factual and legal bases for the claim of invalidity or non-infringement.
3. ***Notice to the FTC.*** To help avoid anti-competitive agreements between generic and brand companies, when a biosimilar applicant contacts a patent holder under the patent provisions of this bill, the contact must be reported confidentially to the Federal Trade Commission.
4. ***Patent Remedies.*** If a patent required to be disclosed is, in fact, not disclosed in response to a request, that patent may not be enforced against that applicant. If a patent is disclosed and is the subject of a notice, but no patent infringement action is not brought within 45 days of notice, or is not maintained through a final decision or dismissal with prejudice, the remedies in any later action to enforce that patent against the submitter of the notice are limited to reasonable royalties.

H. User fees

A company that files an application for a biosimilar biological product must pay a user fee to FDA.