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Biologics Legislation In The 111th Congress

Law360, New York (May 1, 2009) — Two bills have been introduced in the House that aim to create an FDA approval process for follow-on biologics similar to that established for generic drugs in the Hatch-Waxman Act of 1984.

The first bill, H.R. 1427, the "Promoting Innovation and Access to Life-Saving Medicine Act," outlines an approval process that is highly favorable to follow-on biologic companies, whereas the second bill, H.R. 1548, the "Pathway for Biosimilars Act," stakes out a position somewhat more favorable to the innovator biologics industry. A new law could take effect later this year.

Overview of H.R. 1427

Representatives Henry Waxman, D-Calif., Nathan Deal, R-Ga., Frank Pallone, D-N.J., and Jo Ann Emerson, R-Mo., introduced H.R. 1427 on March 11, 2009.

Abbreviated Application Procedure

H.R. 1427 provides an abbreviated application procedure for "biosimilar" and "interchangeable" products. Unlike the Hatch-Waxman Act, the touchstone for abbreviated application eligibility is similarity, not sameness, of the follow-on product to the branded biologic.

According to the bill, a "biosimilar" product has "no clinically meaningful differences" compared to a reference product in terms of "safety, purity, and potency" during treatment.

A product is "interchangeable" if it is biosimilar to a reference product and the risk of switching a patient between the reference product and the follow-on is not significantly greater than the expected risks of continuing to use only the reference product.

The FDA may determine that a product is biosimilar without also finding that it is interchangeable.

Exclusivity Periods

H.R. 1427 provides for exclusivity periods similar to those in the Hatch-Waxman Act, during which the Secretary may not approve new abbreviated applications that refer to an approved product.

For biological products with novel molecular structures, H.R. 1427's exclusivity period is five years. For products that include a "major substance" that has previously been approved in another

application or that is "highly similar" to such a previously approved major substance, the exclusivity period is three years.

A license-holder may extend its exclusivity by six months if it shows that its product has a new disease-treatment application no later than one year before the exclusivity period ends.

However, this extension can be reduced to three months if the combined annual gross sales in the United States for all products containing the major substance and owned by the applicant exceed $1 billion. License-holders may also extend their exclusivity by an additional six months by conducting pediatric studies. The bill also includes an exclusivity period for the first biological product to be deemed interchangeable with a particular reference product.

Whereas the Hatch-Waxman Act provided for only a 180-day exclusivity period for the first generic drug to be marketed, H.R. 1427 prevents any subsequent interchangeability determinations with respect to the same reference product until the earlier of:

a) 180 days after the first commercial marketing of the first interchangeable;

b) one year after a final court decision in a patent infringement action brought against the first follow-on biologic applicant if the decision is in favor of that applicant (or one year after the dismissal of such an action);

c) 36 months after the first interchangeable's approval if the applicant has been sued and the litigation is still ongoing; or

d) one year after the first interchangeable's approval if the first follow-on biologic applicant has not been sued.

Patents: Identification and Challenges

H.R. 1427 establishes procedures for the identification of patents related to reference products that differ substantially from those set forth in the Hatch-Waxman Act. Notably, the bill does not create an equivalent to the Hatch-Waxman Act's "Orange Book."

Pioneers would not publicly list patents related to their products, and follow-on applicants would not be required to serve "paragraph IV"-like certifications. Instead, a follow-on applicant may at any time send a written request to the holder of an approved application for a reference product seeking information on patents relating to the reference product.

Within 60 days, the holder must provide a list of all patents owned by or licensed to the holder that relate to the reference product.

If the holder does not disclose a related patent in response to an applicant's request, the holder cannot later bring an infringement action against that applicant with respect to the omitted patent.

For a period of two years from the initial request, the holder must provide the applicant with an updated list no later than 30 days after the date on which a new related patent issues or a license is obtained.

After submitting an abbreviated application, the applicant may notify the holder of an approved application that it intends to challenge one or more of their related patents, whether or not the patents were identified by the holder.

The notice must include a detailed statement of the bases for the patent invalidity, unenforceability, or noninfringement claims. The notice must also be submitted to the FTC.

Under paragraph (18)(C) of the bill, the patent holder then has 45 days within which to bring an infringement action with respect to the patents referenced in the notice.

If a patent holder does not bring an infringement action against the applicant within the 45-day period following the applicant's notice, the remedies in any subsequent infringement action against the applicant on the noticed patents are limited to reasonable royalties.

Unlike under the Hatch-Waxman Act, there is no 30-month stay of generic application approvals if a patent holder elects to bring an infringement action.

Overview of H.R. 1548

On March 17, 2009, Reps. Anna Eshoo, D-Calif., Jay Inslee, D-Wash., and Joe Barton, R-Texas, introduced the second follow-on biologics bill of the 111th Congress: H.R. 1548.

Abbreviated Application Procedure

H.R. 1548 provides an application procedure for biosimilar and interchangeable products.

The bill provides for a determination of interchangeability of a biosimilar product, if it "can be expected to produce the same clinical result as the reference product in any given patient," and, in the case where the product is administered more than once, if the risk of alternating products is not greater than the risk of using only the reference product.

Exclusivity Periods

Under the bill, a follow-on applicant may not submit an application until four years from the date on which the reference product was licensed. Further, the FDA may not approve a follow-on application until 12 years after the license date.

The approval exclusivity period can be extended under the bill. If, during the first eight years of licensure, the FDA approves the marketing of the reference product for a medically significant new indication, then the approval exclusivity period is extended to 14 years.

The reference product sponsor can also receive an additional six months of approval exclusivity if it completes pediatric studies involving the product and submits reports of the studies to the FDA.

H.R. 1548 also grants exclusivity for the first product deemed interchangeable with a particular reference product.

The bill provides that the FDA shall not make a determination that a second product is interchangeable with the same reference product until 24 months after either the date of the initial commercial

marketing of the first product or the date the first product was deemed interchangeable if it is already being marketed, whichever is later.

Patents: Identification and Challenges

Like H.R. 1427, H.R. 1548 does not create an equivalent to the Hatch-Waxman Act's "Orange Book," but it does establish a procedure that resembles "paragraph IV" certification.

Under the bill, within 30 days of accepting an application, the FDA must publish a notice stating both the reference product identified in the application and contact information for the follow-on applicant.

Also within 30 days of acceptance, the applicant must provide the reference product sponsor with a copy of the application and information about the biosimilar product.

Within 60 days of receiving this information, the reference product sponsor must provide a list of the relevant patents. H.R. 1548 mandates that the sponsor list all "relevant patents" that the sponsor owns, has the right to assert, or "otherwise has an interest" in.

"Relevant patents" include all "patents that could reasonably be asserted against the applicant." For each patent identified, the sponsor must explain why the patent would be infringed and provide the patent's expiration date.

If the product sponsor subsequently acquires or is issued a relevant patent, the sponsor must notify the applicant within 30 days of the acquisition or issuance.

Under paragraph (4)(D), within 45 days of receiving the patent list and related information, the applicant must send a detailed written statement to the sponsor regarding each identified patent.

The applicant must state either that its biologic product will not be marketed until expiration of the identified patent or that the patent will not be infringed, or is invalid or unenforceable.

The bill does not include any deadline by which a sponsor must bring an infringement action.

If, however, an infringement action is brought within 60 days of receiving an applicant's certification and the applicant's product is subsequently found to infringe, then FDA approval of the applicant's product will not be effective until after the relevant patent expires.

Evolution of Follow-On Biologics Legislation

The proposed legislation will weaken patent protection for biologics pioneers. Neither bill affects the safe harbor from infringement for followers' development of data for regulatory approval (35 U.S.C. § 271(e)(1)).

But, whereas the Hatch-Waxman Act provided a 30-month stay of FDA approval during the pendency of patent litigation, the current bills do not provide for such a stay.

In addition, H.R. 1427 and H.R. 1548 require follow-on biologics to be merely similar, rather than identical, to their reference products. A "similarity" standard is a necessary result of biologics' molecular complexity and the fact that they are produced through biological processes.

It would be practically impossible to require follow-on biologics to be "identical" to their reference products. But a "similarity" standard creates the possibility of a follow-on biologic being "similar enough" to obtain abbreviated FDA approval, while still sufficiently different from the reference product to escape patent infringement.

H.R. 1548 compensates pioneers by providing longer periods of marketing exclusivity. This bill strikes a better balance between the short-term desire for cheaper medicines and the long-term need for investment in research and development in this important industry.

Longer exclusivity periods will also provide greater certainty to both pioneers and followers and will likely reduce the prevalence of expensive patent disputes.

The change in the Congressional balance of power following the November 2008 elections may have strengthened supporters of a statute that substantially impairs the rights of biologics pioneers. But lawmakers should bear in mind the long-term public benefits of biologics research and enact a carefully balanced law.

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