

## Client Advisory | March 2010

## New Law! The Biologics Price Competition and Innovation Act of 2009

Last June, we reported on the emerging debate over “follow-on biologics” and noted that it was likely only a matter of time before Congress passed into law a structured pathway for abbreviated FDA approval of such drugs.<sup>1</sup> That time has now come.



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On March 23, 2010, President Obama signed into law the much-debated health-care reform bill known as the Patient Protection and Affordable Care Act (“Healthcare Bill”).<sup>2</sup> The “Biologics Price Competition and Innovation Act of 2009” (“Biologics Act”) is included as a subtitle of the Healthcare Bill, and it creates a framework for FDA approval of follow-on biologics. This new follow-on biologics law bears a conceptual resemblance to the Drug Price Competition and Patent Term Restoration Act of 1984 (more commonly known as the “Hatch-Waxman Act”), which created a path to market entry for generic small molecule pharmaceuticals. The Biologics Act, however, is different in several important respects, most of which reflect the different nature of biologics themselves (complex biologics vs. small molecules) as well as the industries which create them (biotech vs. traditional pharma).

The key provisions of the new Biologics Act are as follows:

The Act uses the term “**biological product**,” for what is commonly called a “biologic” and defines “biological product” as:

- a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings. (Amending 42 U.S.C. § 262(i)).

In addition, the bill defines “**reference product**” to mean the biological product against which a follow-on biologic is evaluated.

### Application/Approval Issues

An application for a follow-on biologic must include the following certifications from the applicant:

- (1) that the biological product is **biosimilar** to the reference product, based upon
  - (a) data from analytical studies; and
  - (b) data from animal studies (including toxicity studies); and
  - (c) data from a clinical study or studies sufficient to demonstrate safety, purity, and potency in one or more “appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product.”
- (2) that the biological product and reference product “utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling” (but only to the extent such mechanism is actually known for the reference product);
- (3) that the conditions of use in the labeling for the proposed biological product have been previously approved for the reference product;
- (4) that the route of administration, dosage form, and strength of the biological product are the same as those of the reference product; and

<sup>1</sup> See “The Follow-on Biologics Debate and the June 2009 FTC Report on Follow-on Biologic Drug Competition,” EAPD Client Advisory, June 2009.

<sup>2</sup> See Pub. L. No. 111-148.

(5) that the facility in which the biological product is manufactured meets standards designed to “assure that the biological product continues to be safe, pure, and potent.”

For a follow-on biologic to be deemed “**biosimilar**” or to achieve “**biosimilarity**,” data must be produced to show that the biological product (a) is “highly similar” to the reference product “notwithstanding minor differences in clinically active components”; and (b) exhibits “no clinically meaningful differences” relative to the reference product in terms of safety, purity, and potency. A biosimilar drug is considered to have a new “active ingredient” compared to the reference product.

An applicant may additionally include information demonstrating that its biological product meets a higher standard, **interchangeability**.

For a follow-on biologic to be deemed “**interchangeable**,” data must be produced to show that the biological product (a) is biosimilar to the reference product; and (b) can be expected to produce the “same” clinical result “in any given patient” as the reference product. Furthermore, if the biological product is “administered more than once to an individual,” it will only be deemed interchangeable if the risk (in terms of safety or diminished efficacy) of alternating or switching between the biological product and the reference product “is not greater than the risk of using the reference product without such alternation or switch.” A biological product that is interchangeable will be considered to have the same “active ingredient” as the reference product.

### Exclusivity Issues

The most hotly contested issue in the passage of the Biologics Act involved length of a statutory exclusivity period for biologics. These exclusivities can be divided into two main categories:

#### Exclusivity for Reference Product

No follow-on biologic application may be submitted until four years from the date on which the

reference product was first licensed by the FDA. No follow-on biologic application may be approved until twelve years from the date on which the reference product was first licensed by the FDA. An additional six months of exclusivity may be obtained for approved pediatric or rare disease indications.

#### Exclusivity for First Interchangeable Biological Product

If a follow-on biologic is approved by the FDA and is deemed to be interchangeable (not merely biosimilar), then the applicant receives the lesser of one year of exclusivity after the date of first commercial marketing or eighteen months of exclusivity after FDA approval vis-à-vis any other approved, interchangeable follow-on biological products. (Note: a somewhat different calculus applies to this exclusivity period if patent litigation involving the first follow-on applicant is not yet resolved.)

### Patent Infringement Issues

An immediately recognizable difference between the Biologics Act and small molecule/Hatch-Waxman frameworks is that there is no “Orange Book” for biologics to list patents that cover the reference product. Instead, the new law requires a process of information sharing between the follow-on biologic applicant and the reference product “sponsor” (typically the patent holder or licensee).

- Within twenty days of notification that its application has been accepted for FDA review, the follow-on applicant must provide limited confidential access to a copy of the application to the reference product sponsor.
- Within sixty days after receiving confidential access to the application, the reference product sponsor must (1) provide the follow-on applicant with a list of patents for which a claim of patent infringement is believed could be reasonably asserted; and (2) identify the patents on this list that the refer-

ence product sponsor would be prepared to license to the applicant (if any).

- Within sixty days after receiving the reference product sponsor’s patent “list,” the follow-on applicant must provide to the reference product sponsor, with respect to each patent on the list: (1) a detailed statement describing the factual and legal basis of the opinion of the applicant that such patent is invalid, unenforceable, or will not be infringed (the equivalent of a Paragraph IV letter under Hatch-Waxman); or (2) a statement that the applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires (the equivalent of a Paragraph III certification). The applicant must also provide a response regarding the patents the reference product sponsor indicates it would be prepared to license.
- Within sixty days after receiving the applicant’s response, the reference product sponsor must (1) provide a detailed statement describing the factual and legal basis for why each listed patent will be infringed; and (2) provide a “response” to the applicant’s statement regarding validity and enforceability. There is no similar requirement under the Hatch-Waxman Act.

After this information exchange period, the parties have two weeks to agree on which patents should be the subject of a patent infringement suit. If agreement is reached, the complaint must be filed within thirty days. If no agreement is reached, then a slightly different procedure is followed, but the complaint must nevertheless be filed in short order. Importantly, there is no thirty month stay akin to the Hatch-Waxman framework. However, the follow-on biologic applicant must provide the reference product sponsor with 180 notice before commercial marketing, thus allowing the reference product sponsor to seek a preliminary injunction against the follow-on biologic entering the market.

## Regulatory Issues

All applications for biological products must now be submitted under Section 351 of the Public Health Service Act, 42 U.S.C. § 262 (as amended). There is limited grandfathering, however, for biological products that are in a “product class” that is the subject of an application which has already been approved under Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355. Such grandfathering will effectively expire in ten years.

## Conclusion

The Biologics Price Competition and Innovation Act of 2009 is a brand new law, with brand new language that will need to be construed by regulatory agencies, courts, and practitioners. The law clearly contemplates that

the FDA will issue guidance (after the requisite notice and comment period) with respect to certain aspects of the new law. How, for example, will the FDA implement the “biosimilarity” designation, which requires that a product be “highly similar” to the reference product “notwithstanding minor differences in clinically active components?” How much and what form of analytical data will be required? How much animal data? How much clinical data? What about the heightened requirements for “interchangeability?” Many other terms within the statute will also need further construction and development. The obvious incentive for follow-on biologic applicants will be to ensure that their product meets the FDA’s criteria for biosimilarity to the reference product, but then to show that their product will be

different enough – either in composition or method of manufacture – so as not to infringe any of the patents covering the reference product.

In addition, the system of patent “information exchange” established by the new law is somewhat of a novelty and will have to be worked out between parties. Given the number and complexity of patents that often cover biologics, early assessment of which patents can viably be asserted is critical.

Edwards Angell Palmer & Dodge will continue to provide updates and analysis on this important new law. The firm has substantial experience in all of the areas that touch on biologics and follow-on biologics – in particular, intellectual property, intellectual property litigation, life sciences, antitrust, and FDA regulatory practices.

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