

DRUG APPROVAL PATHWAY ESTABLISHED FOR BIOSIMILAR DRUGS

On March 23, 2010, President Obama signed the Patient Protection and Affordable Care Act (the “Act”) — health care legislation that includes the establishment of an abbreviated biosimilar biologic drug approval pathway.¹ The term “biosimilar” is often used to describe biologic drugs that are similar, but not identical, to previously approved biologic drugs. Abbreviated biosimilar biologic drug approval is now governed by the provisions set forth in a subtitle of the Act, the Biologics Price Competition and Innovation Act of 2009 (the “BPCIA”).²

The BPCIA stems from years of industry and legislative debate focused on facilitating the introduction of cheaper alternatives to biologic drugs previously approved in the United States. Biosimilar biologic drug applicants and holders of previously approved biologics license applications (“BLAs”) are now governed by BPCIA provisions determining, among other aspects, biologic drug regulatory exclusivity periods and the resolution of patent issues.

Background

An abbreviated drug approval pathway has been available for small molecule drugs in the United States since 1984, when The Drug Price Competition and Patent Term Restoration Act (commonly known as “Hatch-Waxman”) was enacted. Hatch-Waxman does not encompass biologic drugs which are larger and more complex than small molecule drugs and often involve complicated manufacturing procedures that incorporate use of living organisms.

Abbreviated Biosimilar Approval Pathway

The BPCIA establishes biosimilar application requirements (Section A, below), defines which biologic drugs are “biosimilar” and/or “interchangeable” (Section B, below), provides exclusivity periods for new biologics and interchangeable biosimilars (Section C, below), and sets forth a structure governing resolution of patent issues (Sections D-F, below).

A. Application Requirements

The BPCIA requires biosimilar applicants to provide, among other things, analytical studies demonstrating that the biological product is highly similar to the reference product, animal studies (including an assessment of toxicity), and a clinical study or studies (including an assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are “sufficient to demonstrate safety, purity, and potency” of the applicant’s proposed product.³

¹ Patient Protection and Affordable Care Act (the “Act”), Public Law No: 111-148, §§ 1001 *et seq.* (2010).

² The BPCIA is located in Title VII, Subtitle A, §§ 7001 to 7003 of the Act.

³ BPCIA § 7002(a).

B. “Biosimilar” and “Interchangeable”

Under the BPCIA, the scope of similarity (or dissimilarity) permitted for biosimilars will be guided by the definition of “biosimilar” and “biosimilarity” provided in the legislation. These terms are both defined to mean: “(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and (B) [that] there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.”⁴

The BPCIA distinguishes between biosimilars and biosimilars that are also “interchangeable.” For a drug to be “interchangeable,” the FDA must determine that, for a drug administered multiple times, substitution of the applicant’s product for a previously administered approved biologic does not increase risks associated with or decrease the efficacy of treatment. The terms “interchangeable” and “interchangeability” are defined to mean “that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.”⁵

C. Exclusivity

The BPCIA provides a 12-year exclusivity period for a biologic drug first licensed (approved), pursuant to a BLA (a “reference drug”). For the first four years of the 12-year exclusivity period, biosimilar applicants are barred from submitting applications to the FDA. The 12-year exclusivity period may be extended six months for performing pediatric studies.

The BPCIA also provides an exclusivity period for the first approved interchangeable biosimilar biological drug product. The exclusivity period prevents the FDA from making a determination that a subsequent biosimilar relying on the same reference product is interchangeable for any condition of use absent certain events. Specifically, once a first approved interchangeable biosimilar is commercially marketed, the BPCIA provides a maximum one-year period of exclusivity. This period of exclusivity may expire earlier if: (1) 18 months have elapsed since, either a final court decision on all the patents in a suit against the first approved interchangeable biosimilar applicant initiated under the BPCIA patent provisions (an “Action”), or such an Action is dismissed with or without prejudice; (2) 42 months have elapsed after approval of the first approved interchangeable biosimilar and an Action is still ongoing; or (3) 18 months have elapsed after approval of the first approved interchangeable biosimilar and there is no Action.

D. Notification and Exchange of Patent Information

The BPCIA refers to biosimilar applicants as “subsection (k) applicants” (“Applicants”) and to holders of previously approved BLAs for reference drugs as “reference product sponsors” (“Sponsors”).

⁴ *Id.* § 7002(b).

⁵ *Id.*

With regard to notification and exchange of confidential information, an Applicant must provide the Sponsor's designated agent(s), within 20 days after receiving FDA notification that its application has been accepted for review, a copy of the Applicant's application and such other information that describes the process or processes used to manufacture the biological product. Absent an ensuing infringement action and the entry of a protective order, the Sponsor's use of confidential information is limited to making patent infringement determinations. If no action is filed, the Sponsor must return or destroy the confidential information.

Within 60 days of receiving the Applicant's application, the Sponsor must provide the Applicant with a list of patents for which the Sponsor believes an infringement claim could reasonably be asserted and identify any such patents that are available for license to the Applicant. In turn, the Applicant, within 60 days thereafter, may provide the Sponsor with a list of additional patents that the Applicant believes could reasonably support a claim of patent infringement. The Applicant must also provide the Sponsor, with either a detailed statement of "the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of" Applicant's product, or a statement that it does not intend to commercially market its product before the date the patent expires. Then, within 60 days thereafter, the Sponsor must provide the Applicant with a detailed statement that describes the factual and legal basis of the Sponsor's opinion that such patent(s) will be infringed by the commercial marketing of the Applicant's product.

Thereafter, the parties must engage in good faith negotiations to agree on which, if any, of the listed patents are to be part of an infringement action. Failing agreement within 15 days, the Applicant must provide notice to the Sponsor of the number of patents that it believes should be the subject of a patent infringement action. Within five days thereafter, the Applicant and Sponsor must simultaneously exchange lists of patents that each believes should be the subject of a patent infringement action. The Sponsor must then bring a patent infringement action within 30 days with respect to each patent as agreed during negotiations or as identified on the lists simultaneously exchanged by the Sponsor and the Applicant.

The BPCIA also provides procedures for patents newly issued to or licensed by the Sponsor to be subject to provisions governing information exchange and potential suits for infringement.

E. Limitations on Preliminary Injunctions

The BPCIA provides that the Applicant must give notice to the Sponsor at least 180 days before the date of first commercial marketing of its licensed product. Upon receiving this notice, and before the first commercial marketing, the Sponsor may seek a preliminary injunction to prohibit the Applicant's commercial manufacture or sale of its product until the court decides the validity, enforcement, and infringement issues of any patents originally identified in the patent list of either party that were not included on any agreed upon or simultaneously exchanged patent list.

F. Declaratory Judgment Provisions

If an Applicant complies with the BPCIA provisions, no patent-based declaratory judgment may be sought until after the Applicant has provided the Sponsor with at least 180 days' notice regarding the date of its first licensed commercial marketing. However, if an Applicant does not provide a copy of its application to the Sponsor as required under the BPCIA, the Sponsor may file a declaratory judgment action based on any patent. Alternatively, the Applicant's failure to comply with certain other provisions of the BPCIA may permit the Sponsor to file a declaratory judgment action based on patents listed on its original or any supplemental patent listing.

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April 1, 2010

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