# Obama's Healthcare Law Paves the Pathway for Approval of Biosimilar Drugs

The Patient Protection and Affordable Care Act was signed into law by President Obama on March 23, 2010 (as Pub. L. No. 111-148). With it come some important changes for the biotechnology industry, particularly as contained in a subtitle known as the Biologics Price Competition and Innovation Act of 2009.

Incorporating provisions contained in earlier bills introduced in the Senate by the late Edward Kennedy (D-MA), and in the House by Anna Eshoo (D-CA), Jay Inslee (D-WA) and Joe Barton (R-TX), the Biologics subtitle creates an approval pathway for follow-on biologics, and awards 12 years of market and data exclusivity to innovator products. It also contains several other key provisions, but it remains to be seen how it will be implemented and applied.

## Approval Pathway for Biosimilars

The Biologics subtitle amends Section 351 of the Public Health Services Act, to authorize the FDA to approve abbreviated biological product license applications. Such abbreviated applications are for "biosimilar" products that are "highly similar to the reference product notwithstanding minor differences in clinically inactive components" and where "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."

Besides the submission of appropriate analytical, animal and clinical studies, to demonstrate biosimilarity, a follow-on applicant must also show that its product utilizes the same mechanism(s) of action (to the extent known for the reference product), has the same condition(s) of use, and has the same route of administration, dosage form and strength as the reference product, and that it will be manufactured in a facility that meets applicable standards.

If a biosimilar product is "expected to produce the same clinical result as the reference product in any given patient," and would not create additional risk if a patient is switched to that product, it may be determined to be "interchangeable." An interchangeable product "may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product."

## Twelve-Year Exclusivity Period

Although the subsection makes way for approval of follow-on biologics, submission of a biosimilar application is prohibited until four years after the reference product was first licensed.

Furthermore, approval of a follow-on biologic is not made effective until the expiry of a marketing and data exclusivity period guaranteed to the reference product sponsor. As enacted, follow-on biologics will have to wait "until the date that is 12 years after the date on which the reference product was first licensed." Six-month exclusivity extensions are available if the reference product is subsequently approved for pediatric use, or if the reference product is approved for a "rare disease or condition."

The length of the exclusivity period had been heavily debated. The Generic Pharmaceutical Association lobbied for five years of exclusivity. Following a proposal by Representative Henry Waxman (D-CA) for a five-year period, the White House pushed for a "generous compromise" of seven years. The Biotechnology Industry Organization sought 12–14 years. The Federal Trade Commission responded with a report asserting that 12–14 years is unnecessary to promote innovation. The twelve-year exclusivity period ultimately enacted is the same as that contained in the original provisions in the Senate bill introduced by Senator Kennedy and in the House bill by Representative Eshoo.

The first "interchangeable" biological product is also awarded an exclusivity period lasting from 12 to 42 months, depending on the timing of approval and commercial marketing, and the status of any infringement litigation with the reference product sponsor. During this exclusivity period, no subsequent biological product can be determined to be interchangeable with the referenced product for any condition of use.

## Additional Provisions

An additional notable provision of the Biologics subtitle is its creation of a prelitigation process between the follow-on applicant and the reference product sponsor. Instead of enacting a parallel to the "Orange Book" created by Hatch-Waxman, the Biologics subtitle creates a patent information exchange procedure where the reference product sponsor provides each follow-on applicant directly with "a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted." This list must be turned over within 60 days of receiving a copy of the follow-on application, which the applicant is required to provide no later than 20 days after the application is accepted for review.

After the applicant replies with a statement "concerning the validity and enforceability" of the patents, the reference product sponsor must provide, on a claim-by-claim basis, a "factual and legal" statement for why the patents are infringed, and "a response to the statement" made by the applicant. Subsequently, the reference product sponsor and follow-on applicant must engage in good-faith negotiations to determine which, if any, patents will be the subject of an infringement action. If no agreement is reached, the subtitle sets forth a specific procedure for initiating infringement litigation. Provisions are also made for preliminary injunction petitions and declaratory judgment actions.

Despite this new statutory pathway for approval, follow-on biologics face higher market-entry barriers than small-molecule generics. The complexity of biologics results in higher product development and manufacturing costs, in addition to greater regulatory risk, as interchangeability will likely be more difficult to achieve. Therefore, it remains to be seen whether passage of the Biologics Price Competition and Innovation Act of 2009 will mirror the impact that the Hatch-Waxman Act had on the pharmaceutical industry.

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