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Biosimilar Law and Regulation: An Essential Guide

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By Erika F. Lietzan, Partner, Covington & Burling LLP

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About the Author

Erika Lietzan is a Partner in the food and drug and government affairs practice groups at Covington & Burling LLP. She specializes in U.S. and ex-U.S. regulation of drugs and biologics and has been working on biosimilar issues for nearly ten years. She was deeply involved in the stakeholder discussions that began in 2005 and eventually led to enactment of the Biologics Price Competition and Innovation Act in 2010, and she and two colleagues at Covington prepared an exhaustive informal legislative history of the statute that appeared in the December 2010 issue of the *Food & Drug Law Journal*. She speaks frequently, including overseas, on global developments relating to biosimilars. In addition to biosimilars, her areas of special focus at this time include the Hatch-Waxman Amendments; data and market exclusivities (including 180-day exclusivity and pediatric exclusivity); supply chain issues (e.g., counterfeiting, pedigrees, importation and online pharmacy); and drug safety (e.g., risk management, labeling changes and pharmacovigilance). Lietzan is past chair of the Biotechnology Committee of the American Bar Association, and she is currently a member of the FDLI Board of Directors and an elected member of the American Law Institute.

About this Monograph

The Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created a pathway for approval of biosimilar and interchangeable biological products, became law on March 23, 2010. The statute does not require the Food and Drug Administration (FDA) to issue implementing regulations or guidance, although the agency will almost certainly eventually issue both. To date, however, FDA and agency officials have said very little publicly about their interpretation of the statute. In October 2010, the agency opened a public docket for comment, listing nearly two dozen questions on which it sought input. In November, the agency held a two-day public hearing under part 15 of its regulations, asking witnesses many of the same questions but also raising new issues for consideration. These docket and hearing questions constitute most of what we know about the agency's thinking on the statute.

This monograph is intended to provide lawyers practicing in this area with a tool for planning in the absence of clear guidance from FDA. It describes the positions taken by FDA with respect to approval and regulation of biosimilars during the multi-year stakeholder process that eventually led to enactment of the legislation. It describes the provisions of the statute. It identifies and explains the issues and questions raised by FDA to date and places them, where possible, within the context of prior agency statements. It then summarizes the positions taken by stakeholders in November and December on those issues and questions.

After reading this monograph you will, among other things:

- Understand how and why statements FDA has made over the years about proteins approved under the Federal Food, Drug, and Cosmetic Act (FDCA) may shed light on its implementation of the BPCIA.
- Understand the differences between, and relevance of, Dr. Woodcock's 2007 article in *Nature Reviews Drug Discovery*, Secretary Leavitt's 2007 letter to the Senate, and Dr. Torti's 2008 letter to the House, on biosimilar issues.
- Understand the positions taken by stakeholders on the new definition of "biological product" and on the appropriate scope of the pathway at this point in time.
- Understand the debate over the use of data from clinical trials involving comparisons with innovative biological products not approved by FDA.
- Understand the positions urged on FDA with respect to interpretation of the "first licensure" provision (relating to exclusivity), including possible meanings of the phrase "related entity."
- Understand the discussion in the FDA docket over the current capabilities of analytical technology to demonstrate structural similarity of biological products.
- Appreciate the positions taken by stakeholders on the role of clinical pharmacokinetic and pharmacodynamic studies and whether, and when, studies with efficacy (clinical) outcomes are necessary.
- Understand the legal and regulatory structure that frames the issue of nonproprietary names for biological products, FDA's prior statements on naming, and the positions taken by stakeholders on this contentious issue.
- Appreciate the relevance of the history of therapeutic equivalence ratings at FDA and understand the many issues FDA faces in implementing the interchangeability provisions of the BPCIA.
- Understand the key differences between the patent litigation process under BPCIA and the patent litigation process under the Hatch-Waxman Amendments.
- Understand the role that some stakeholders believe FDA should play in implementation of the patent provisions of the BPCIA.

I. Introduction

The Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created a pathway for approval of biosimilar and interchangeable biological products, became law on March 23, 2010.[1] The statute does not require the Food and Drug Administration (FDA) to issue implementing regulations (or amend its existing regulations) or to issue guidance, although the agency will almost certainly eventually do both. Indeed, the agency's recent budget request suggests that it plans both, and the Commissioner of Food and Drugs recently signaled that proposed regulations may be released in the near term.[2]

To date, however, FDA and agency officials have said very little publicly about their interpretation of the provisions that the agency must implement. In October 2010, the agency opened a public docket for comment, listing nearly two dozen questions on which it sought input.[3] In November, the agency held a two-day public hearing under part 15 of its regulations, asking witnesses many of the same questions but also raising new issues for consideration.[4] These docket and hearing questions constitute most of what we know about the agency's thinking on the statute. Some officials have also been quoted in the trade press on the new law, after having given speeches or press interviews, but it is difficult to interpret these comments in isolation.

This monograph attempts to explain the new requirements within this challenging landscape. Section II provides a brief background on federal regulation of biological drugs since 1902. It also provides a history of FDA's views and statements with respect to biosimilars, including during the legislative process from 2006 to 2010. Section III discusses the regulatory provisions of the statute, and Section IV discusses the patent provisions. In addition to summarizing the statute, these sections discuss questions raised by FDA and positions taken by stakeholders. No attempt is made to attribute positions to specific stakeholders, and not all perspectives are captured. On some issues, additional background is provided. Where relevant and helpful, the approach taken in Europe or other jurisdictions is noted.

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[1] Patient Protection and Affordable Care Act, Pub. L. No. 111-148, Title VII, Subtitle A, 124 Stat. 119, 804-821. The terms "biosimilar" and "interchangeable" are defined in the statute and discussed in Section III of this monograph.

[2] Department of Health and Human Services, FDA FY2012 Congressional Justification, at 38-39; Catherine Larkin, *FDA's Rules for Copying Amgen, Roche Drugs* Coming '*Very Soon,*' Bloomberg, Feb. 18, 2011.

[3] 75 Fed. Reg. 61,497 (Oct. 5, 2010) (Notice of public hearing; request for comment).

[4] 21 C.F.R. part 15. The transcripts from this hearing can be found on the regulations.gov website.