Panacea or Poison Pill?
Making Sense of the New Biosimilars Law

By
James N. Czaban
Karin A. Hessler
Matthew J. Dowd

Submitted by
James H. Wallace, Jr.
Wiley Rein LLP
Washington, D.C.
Panacea or Poison Pill? Making Sense of the New Biosimilars Law

BY JAMES N. CZABAN, KARIN A. HESSLER, AND MATTHEW J. DOWD

I. INTRODUCTION

After more than a decade of debate and mounting demand for lower-cost “generic” versions of biotechnology products, Congress on March 21 passed the Biologics Price Competition and Innovation Act (the Biosimilar Act), which is included as Title VII of the Patient Protection and Affordable Care Act (the Healthcare Reform Act). The Biosimilar Act creates what is intended to be a streamlined development and FDA approval pathway for competing versions of already-marketed biologic drug products, with the goal of lowering prices through increased competition in the fastest growing and arguably most important segment of the health care industry. However, the new law already has been subject to criticism from longtime biosimilar advocates for both its complexity and its perceived bias toward innovator biologics manufacturers.

The act is indisputably complex, and many important details are left undefined or open-ended. FDA and the courts will be forced to take on significant burdens in interpreting and implementing the new law. It likely will be several years before even the basic elements of the law are elucidated, and if experience under the Hatch-Waxman amendments to the Federal Food,
Drug, and Cosmetic Act (FDCA) is any guide, specific disputes under the new law likely will continue to arise for decades.

This article provides a brief overview of the history leading up to passage of the Biosimilar Act, discusses in detail both the FDA regulatory and patent litigation provisions of the act (with comparisons and contrasts to the Hatch-Waxman scheme), probes potential interpretations of key provisions, and offers practical strategic considerations both for companies seeking to pursue product approvals under the new law, and for companies whose products now may face increased competition from follow-on products.

II. BACKGROUND

A. Biologics are Different. Under the Public Health Service Act (PHSA), biologics are defined to include articles composed of "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings."2 FDA defines the term "analogous" broadly3 such that the term "biologic" also includes, among other things, therapeutic protein products, monoclonal antibodies, and immunoglobulin products. As the term suggests, biologics are derived from living organisms, and they are much larger and more complex than traditional chemical pharmaceuticals. As a result, it is often difficult if not impossible to precisely "characterize" or replicate the structure and composition of the biologic molecule.4

Like pharmaceuticals, FDA approval of an innovator biologic product requires extensive clinical studies, along with a validated and consistent manufacturing process, to prove the safety and efficacy of the product.5 For traditional drugs, Hatch-Waxman only applies to drugs that were originally approved pursuant to a new drug application (NDA) under section 505(b) of the FDCA. Because biologics are approved pursuant to biologics license applications (BLA) under the PHSA, prior to the enactment of the Biosimilar Act, no abbreviated pathway existed for the approval of "generic" versions of biologics.

2 42 U.S.C. § 262(i).
3 21 C.F.R. § 600.3(h).
4 For this reason, the term "generic biologic," with its connotations of exact product duplication, has fallen into relative disuse, even among proponents of a follow-on biologic approval pathway.
5 Under the PHSA, biologics must be shown to be "potent" rather than "effective," but the two terms are, in regulatory practice, essentially synonymous. See 21 C.F.R. § 600.3(s) (defining "potency").
6 "Bioequivalence" is defined as "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study." 21 C.F.R. § 320.1.

B. The Legislative Pathway to a Biosimilar Approval Process. The drive for a biosimilar approval pathway gained momentum with a flourish of legislative activity in Congress in 2007-2008. Numerous versions of bills with competing approaches to critical issues were proposed in the House and the Senate. Significant debates centered on potential data and market exclusivity for innovator biologics and the concept of biosimilarity versus interchangeability. At one point it appeared that a compromise deal had been reached, but the effort eventually stalled due to friction between key members of Congress and declining support from the generic industry which hoped for a better bill under a potential Democratic administration after the 2008 elections.

The window for biosimilar legislation reopened with the election of President Obama and the push for health care reform legislation. The president and congressional Democrats sought to include biosimilars legislation in the health care reform bill to help subsidize the significant costs associated with health care reform.6 However, the biosimilar provisions ultimately included in the health care reform bill tracked the approach advocated by Rep. Anna Eshoo (D-Calif.) whose Silicon Valley district includes many biotechnology companies. In many key respects this version was seen as far less favorable to the generic industry than the compromise version nearly passed prior to the 2008 elections. The Biosimilar Act became law on March 23, when the president signed the health care reform act (§ PLIR 390, 3/26/10).

The Biosimilar Act has two main sections dealing with (i) the regulatory standards and procedures for approval of follow-on biologic products, including regulatory exclusivity periods for innovator and follow-on biologic products, and (ii) complex rules and procedures for identifying and resolving patent disputes involving proposed follow-on products. These two interrelated sets of issues are addressed in the following sections.

III. OPPORTUNITIES AND OBSTACLES ON THE REGULATORY PATHWAY

A. Biosimilarity and Interchangeability

The Biosimilar Act creates a regulatory scheme for two types of generic biologics: "biosimilars" and interchangeable biologic products. Under the act, a generic product can be approved as "biosimilar" to a reference (brand name) biologic product if it is shown to be "highly similar to the reference product notwithstanding minor differences in clinically inactive components" and "there are no clinically meaningful differences between the [biosimilar] biological product and the reference product in terms of safety, purity, and potency of the product."7 A biosimilar biological product can be deemed "interchangeable" if "the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product."8

1. "Biosimilar"—Approval Lite? To meet the baseline criteria for approval of a follow-on biologic, a company

8 The cost savings potential of the bill was vigorously debated, with the Congressional Budget Office estimating $6 billion to $7 billion in savings over 10 years, and the generic industry arguing that the savings could be twice as great.
9 42 U.S.C. § 262(i)(2).
10 42 U.S.C. § 262(i)(3).