Five years ago, the Federal Trade Commission (FTC) waded into the debate regarding the benefits and potential competition issues posed by the introduction of “follow-on biologics.” Now, some three years after Congress provided a pathway for approval of such products, the FTC is jumping back in, as to date no follow-on biologic has been approved by the U.S. Food and Drug Administration (FDA), and new issues have emerged that could delay the introduction of such products.

The FTC appears to be concerned that such issues “may impact the development of, and competition for, follow-on biologics.” and thus has scheduled a workshop on December 10 to examine these issues. This WSGR Alert reviews the current state of play regarding follow-on biologics and frames some of the topics to be evaluated by the FTC in December.

What Are Biologics?

Biologics, which include therapeutic proteins, vaccines, monoclonal antibodies, allergens, and gene therapies, represent some of the most significant—from both a clinical and financial standpoint—pharmaceutical products in the United States today. Biologics are “typically larger and more structurally complex molecules,” and unlike traditional or “small-molecule” pharmaceuticals, which are created through chemical synthesis that can be easily reproduced, biologics are cultivated from living organisms, and production generally requires more difficult and expensive processes and techniques to ensure consistent production. Biologic drugs have had remarkable success in the treatment of patients with many common diseases and disorders such as cancer, diabetes, multiple sclerosis, arthritis, and anemia. At the same time, biologics remain one of the most expensive categories of drugs. According to the FTC, the cost of one year of treatment can range from $50,000 to $250,000.

Follow-on biologics are substantially similar to an approved biologic product, and as such, permit an applicant (who is seeking FDA approval of the biosimilar product) to rely on certain existing scientific knowledge about the safety and effectiveness of the approved reference drug in their application for approval. Follow-on biologics fall into two categories—biosimilars and interchangeable biologic drugs. Biosimilars are biologic drugs that are not completely identical to the previously approved brand-name versions, but that are substantially similar to the branded drug such that the same clinical outcome can be expected, “notwithstanding minor differences in clinically inactive components.” Interchangeable biologics (a follow-on biologic product that may be substituted for the brand biologic), on the other hand, must satisfy more rigorous requirements, producing the same clinical result in any given patient. Manufacturers of interchangeable biologics must also prove that switching from the reference drug to the follow-on biologic, or alternating between the two, carries no greater risk of harm than continuing to take the reference drug without interruption.

In addition to the structural differences outlined above, biologic drugs, unlike traditional small-molecule pharmaceuticals, are not regulated under the Hatch-Waxman Act of 1984, and are therefore not subject to the act’s accelerated FDA approval process. Biologics are also not covered by state laws that allow pharmacists to automatically substitute generics for brand-name drugs. These provisions are credited with creating

5 § 262(i)(2).
6 Id.
Creating a Regulatory Pathway for Follow-On Biologics

In November 2008, the FTC weighed in on this debate as well, holding an all-day roundtable to explore the introduction of an approval process for follow-on biologics. Five separate panels discussed the likely market effects of follow-on biologic entry, likely competitive effects of reference product regulatory exclusivity, patent issues, the effect of regulatory incentives, and patent resolution. Following the roundtable, the FTC issued a report entitled “Emerging Health Care Issues: Follow-On Biologic Drug Competition” that recommended introduction of a legislative process for an abbreviated FDA approval pathway for follow-on biologics.1

In its report, the FTC concluded that competition in the biologics market would more closely resemble brand-to-brand competition than the brand-to-generic competition experienced in the small-molecule drugs market, and predicted that follow-on biologic competition, although meaningful, would be less vigorous than generic-drug competition.2 As such, the FTC opposed proposals for both the 12-to-14-year exclusivity period for pioneer biologics and the pre-approval patent dispute resolution procedures that were proposed by the manufacturers of pioneer biologic drugs.3 The FTC did, however, call for an introduction of an abbreviated pathway and deemed it “an efficient way to bring [follow-on biologics] to market because of the time and cost savings it provides.”4 The FTC also predicted that resulting price competition between follow-on biologics and reference drugs would be “likely to lead to an expanded market and greater consumer access.”5

In June 2010, Congress passed the Biologics Price Competition and Innovation Act (BPCIA), which created an abbreviated regulatory pathway for FDA approval of follow-on biologics. The BPCIA is different from the Hatch-Waxman Act in several respects.6 Regardless of the differences, the purpose was largely the same: allowing approval of generic biologic medicines in order to improve competition in the biologics market and thereby reducing the cost of these expensive medicines for consumers. The BPCIA distinguishes between biosimilars and interchangeable biologics, as defined above.

Namely, a drug can be approved as biosimilar notwithstanding minor differences in clinically inactive components.

Whether a biologic is approved as “biosimilar” or “interchangeable” affects the substitution of these drugs. Although interchangeable biologics “may be substituted for the reference biologic without the intervention of the [prescribing] health care provider” under the BPCIA, the act is silent as to substitution of biosimilars.

Current State of Biologics Competition

Despite the great intentions of the BPCIA, in practice, it has had limited effect on competition from follow-on biologics. In fact, since the introduction of the BPCIA, no follow-on biologic has received FDA approval via the abbreviated pathway, although several applications are currently pending review by the FDA. Additionally, several new public policy issues have emerged and could potentially further delay introduction of such products.7 In particular, manufacturers of brand-name biologics have pressed for the introduction of legislation that could limit the adoption of follow-on biologics, urging that patient safety demands more rigorous review of the substitution processes and more granular naming conventions.8 For example, pharmaceutical companies argue that only interchangeable biologics should be substituted. Many of the proposed state bills also require patient consent for substitution.

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2 FTC Follow-On Biologics Report executive summary at ii.
3 Id. at iii-v.
4 Id. at v-vi.
5 Id. at v-vii.
6 Id. at vi.
7 Id. at vii.
8 Assessments of biosimilarity differ to accommodate the difference in manufacturing and development processes for biologic drugs. Additionally, the BPCIA includes a 12-year exclusivity period for the innovator drug, and also includes IP provisions that create a scheme for confidential information exchange with regard to patent rights. Unlike the Orange Book listings available under the Hatch-Waxman Act, the BPCIA puts the onus on the parties themselves to exchange such information.
or for the pharmacist to inform the patient's physician when a switch is made and for a record of that substitution to be maintained for several years. 16

Proponents of these measures argue that they are necessary to ensure tracing in cases of safety problems. To date, five states have enacted legislation specifically addressing follow-on biologics—Florida, North Dakota, Oregon, Utah, and Virginia.17 Of the five, North Dakota, Oregon, Virginia, and Utah have passed the type of legislation sought by brand-name biologic manufacturers. Notably, the Virginia, Oregon, and Utah laws will all expire by 2016, likely before the relevant follow-on biologics become available.18

In a sixth state, California, the bill was passed, but subsequently vetoed by the governor. The California bill allowed only interchangeable follow-on biologics to be substituted by pharmacists, and required pharmacists to notify both the patient and the patient’s doctor whenever a follow-on biologic was dispensed.19 Introduction of these provisions could have reduced the likelihood of follow-on biologic adoption and the financial incentive for the development of these drugs. Additionally, commentators have pointed out that varying regulatory barriers among different states may deter follow-on biologic competition.20

The naming convention for follow-on biologics is also being debated. Aside from a drug’s proprietary brand name, drugs also carry a non-proprietary active ingredient name, which the FDA has authority to determine.21 There exists significant debate about whether follow-on biologics should bear the same non-proprietary name as the reference drug. The FTC has stated that a drug's name can have a substantial impact on a physician's or patient's acceptance of the generic. If a follow-on biologic has a different non-proprietary name than the branded-drug, concerns about the interchangeability or safety of the generic are heightened. As such, the naming of these follow-on biologics could impact competition significantly. Safety concerns persist, however, as biologic industry representatives have stated that “the absence of adequate ‘track and trace’ systems for biologics required different [follow-on biologics] and [branded] biologic proprietary names in order to gather and differentiate adverse effects caused by the use of branded biologic or [follow-on biologic] products.”22

**FTC Is Taking a Second Look at Follow-On Biologics**

Given the considerable debate over state restrictions on substitution and the uncertainty over naming conventions, the FTC has elected to re-examine follow-on biologics and the competitive issues that surround their introduction. A workshop entitled “Follow-on Biologics: Impact of Recent Legislative and Regulatory Naming Proposals on Competition” will be held December 10, 2013. The FTC is planning to examine current and proposed state legislation and naming conventions, specifically seeking an approach that adequately balances the facilitation of competition and the protection of patient health and safety. An FTC report accompanying the agency’s announcement of the workshop and request for comments sets out a helpful framework for the discussion, which will include an examination of, and comparison with, traditional small-molecule generic drug competition and the experience of foreign regulatory systems that currently facilitate follow-on biologic competition.

Specifically, the FTC workshop will address the rationale behind proposed state legislation and how such legislation could affect the development of biosimilar competition; the likely competitive impact of an “interchangeable” designation for follow-on biologics; the compliance costs associated with state substitution legislation and the resulting effect on competition; the possibility of an FDA publication akin to the Orange Book for follow-on biologics and its potential effect on substitution; and the potential usefulness of a model state substitution law. With respect to naming conventions, the workshop will focus on the experience under Hatch-Waxman with encouraging physicians and patients to switch to follow-on biologics, and how naming conventions can affect this; how regulatory authorities in other jurisdictions approach the naming of follow-on biologics; how the use of prefixes or suffixes affects the use and management of follow-on biologics; how the naming of...
follow-on biologics affects track and trace procedures and other pharmacovigilance systems; and whether the use of nonproprietary names generally enhances or detracts from competition and consumer protection.

For additional information about follow-on biologics, the FTC’s upcoming workshop, or any related matter, please contact Seth Silber, Valentina Rucker, or Roisin Comerford at Wilson Sonsini Goodrich & Rosati.