

Client Advisory | June 2009**The Follow-on Biologics Debate and the June 2009 FTC Report on Follow-on Biologic Drug Competition**

On June 10, 2009, the Federal Trade Commission released a detailed report entitled: “Emerging Health Care Issues: Follow-on Biologic Drug Competition.”¹ The FTC Report is important because it provides the most current government-sector analysis of the U.S. biologics market and the FTC’s recommendations for legislation designed to allow for “follow-on” versions of such drug products. The FTC Report suggests that legislation granting the FDA the authority to approve follow-on biologics is an “efficient” way to bring these products to market. There is considerable tension, however, between the FTC’s recommendations and the two follow-on biologics bills recently introduced in Congress.



Thomas H. Wintner
Associate

Background

While there is some debate as to all of the classes of molecules encompassed by the term “biologic,” there is general agreement that biologics – also known as “biologics” or “biopharmaceuticals” – are large, complex macromolecules derived from living matter or manufactured in living cells using recombinant DNA technologies. As such, they are to be distinguished in the pharmaceutical world from their small-molecule counterparts, which are typically synthesized in a laboratory via traditional chemical synthesis. It is because of this distinction that federal regulation of biologics and their follow-on counterparts has become a hot topic.

A path to market entry for generic small molecule pharmaceuticals has existed since 1984, when the Drug Price Competition and Patent Term Restoration Act – now referred to more commonly as the Hatch-Waxman Act – created the framework for approval of Abbreviated New Drug Applications by the FDA. In the readily growing and maturing segment of biologics, however, no such abbreviated regulatory pathway exists.² This is due to several factors:

The first, and most important, concerns safety and therapeutic equivalence, both of

which are largely within the purview of the FDA. Given the molecular complexity of biologics relative to their small molecule counterparts, as well as the fact that biologics are manufactured in living organisms rather than in a traditional chemical laboratory, it is much more difficult – and in most instances impossible – for a follow-on manufacturer of a biologic to create a product that is 100% identical to its branded counterpart (hence the term “biosimilar” instead of “generic”). Thus, even if a follow-on biologic is purportedly “similar” to a biologic already approved for the U.S. market, the follow-on biologic is likely to be different enough to have a distinct pharmacological profile.

The second is largely economic: given the relative immaturity of the biologics industry, there remain questions as to (a) how much time and money are generally required to bring an innovator’s product to market, and thus (b) what sort of protections should be given to innovators in order to maintain and further promote the current state of biologics innovation. These protections must be balanced against the potentially anticompetitive restrictions that they might impose on would-be follow-on biologics manufacturers.

The third factor relates to intellectual property law. While there is no shortage of patent litigation with respect to biologics, there remain enough uncertainties in these outcomes that it is difficult to pinpoint how much regulatory protection should be given to biopharmaceutical innovators in addition to any patent protection they may enjoy.

Despite the above hurdles, however, most agree that it is only a matter of time before Congress passes into law a structured pathway for abbreviated FDA approval of follow-on biologics. Indeed, President Obama specifically mentioned this as a priority in his first federal budget. Immediately following President Obama's announcement, the two legislators who had been the driving force behind follow-on biologics legislation in previous years, Rep. Henry Waxman (D-Cal.) and Rep. Anna Eshoo (D-Cal.), introduced 2009 versions of their respective bills.³ Both bills have been submitted to committee.

The Role of the FTC in the Follow-On Biologics Debate

The FTC has taken on a role as an important regulatory player in the follow-on biologics debate. This is not surprising, as biologics are the fastest growing segment of the pharmaceutical industry, having generated approximately \$60 billion in global prescription sales in 2006 and \$75 billion in 2007. By 2010, it is estimated that nearly half of newly approved medicines will be biopharmaceuticals. On top of this is the fact that in 2005 the European Union created a framework for approval of follow-on biologics, and several U.S. companies are now geared up to market their follow-on biological pharmaceuticals in Europe, with hopes that the legal and regulatory environment will change in the U.S. within the next few years. In short, given the burgeoning size of the biopharmaceuticals market, and the intricate issues of competition raised by the market entry of follow-on biologics, the FTC stands to play a significant role in shaping any legislation in this arena.

On November 21, 2008, the FTC held a Roundtable entitled: "Follow-on Biologic Drugs: Framework for Competition and Continued Innovation."⁴ The FTC Roundtable brought together some of the nation's authorities on new and follow-on biopharmaceuticals. The agenda included topics about which the FTC had already posed questions for public comment, including:

- Likely market effects of follow-on biologic drug competition;
- Likely competitive effects of reference product regulatory exclusivity;
- Biotechnology patent issues; and
- Likely competitive effects of follow-on biologic regulatory incentives.

The FTC continued to receive comments on the above topics until December 22, 2008. On June 10, 2009, the FTC released its full report on those topics.

The 2009 FTC Report on the Follow-On Biologic Competition

The conclusions contained within the 2009 FTC Report are striking, particularly when compared to the follow-on biologics legislation currently on the table.

The primary conclusion of the FTC Report is that competition between innovator (also referred to as "pioneer" or "branded") and follow-on biologics is much more likely to resemble brand-brand competition than brand-generic competition in the small-molecule arena under Hatch-Waxman. According to the FTC, this is based in large part on:

- The empirical result from the European market (where an abbreviated pathway for follow-on biologics has existed since 2005), and to a lesser extent from the U.S. market, that market entry of follow-on biologics has not resulted steep price discounting, or in rapid loss of innovator market share.
- The economic reality of a company having to develop the manufacturing capacity for biologics, which is considerably more involved than for small-molecule drugs, as well as the likely cost of FDA approval of the follow-on product, even under

some sort of abbreviated regime. The FTC estimates that between \$100 to \$200 million dollars is required for the development and approval of a follow-on biologic drug, as compared with \$1 to \$5 million for small molecule generic drugs.

- The likely impossibility of true "interchangeability" between a follow-on biologic product and its branded counterpart (as compared to the small molecule world, where interchangeability is the norm), as well as the related questions of safety and efficacy variations between "similar," but not identical, versions of a given biologic drug.

Based on this primary conclusion, the FTC predicts that only well-established companies with substantial resources, whether traditionally labeled as "branded" or "generic," will be able to enter into the market for follow-on biologics.⁵ Furthermore, the FTC suggests that the following ancillary conclusions can be drawn:

First, a long (*i.e.*, 12- to 14-year) regulatory exclusivity period is unnecessary to promote innovation by pioneer biologics manufacturers, if any exclusivity period is required at all. The Report states that (a) "there is very little data to suggest that biologics drugs under development are likely to be unpatentable," and (b) "there is no evidence that patents claiming a biologic drug product have been designed around more frequently than those claiming small-molecule products." Given existing incentives in the form of patent protection and market-based pricing for biologics, argues the FTC, data exclusivity periods are superfluous and hence anti-competitive. The Report does suggest, however, that "to the extent there are new biologic molecules that cannot obtain patent protection, an exclusivity period may be warranted."

Second, pre-approval resolution of patent disputes – *i.e.*, resolution of patent disputes prior to FDA approval of the follow-on product – is not necessary in the biologics arena. According to the FTC, the "large companies with substantial resources" that will

be entering the follow-on biologics market will be able to understand the risks of launching their product “at risk,” and will be able to pay damages if they are wrong. The Report further notes that biologics are covered by “more and varied” patents than small-molecule drugs, and thus their resolution prior to FDA approval would take even longer than under the current Hatch-Waxman scheme, thus delaying benefits to the consumer.

Third, follow-on biologics manufacturers will not need additional incentives vis-à-vis their competitors to develop their products. This follows directly from the FTC’s assumption that pioneer manufacturers will face

substantially less competition from follow-on biologics than they face in the small molecule arena. Thus, according to the FTC, any legislation akin to the 180-day exclusivity period under Hatch-Waxman for “first to file” generics is simply not necessary for follow-on biologics.

Further Developments

In view of the fact that both of the current biosimilars bills provide for some amount of regulatory exclusivity (both on the front end for pioneer manufacturers and on the back end for “first” follow-on manufacturers), initial congressional response to the FTC Report has largely been negative.⁶ Venture

capitalists and other investors in biopharmaceutical companies likely will react similarly, and the prospect of no exclusivity might well inspire them to put their investments elsewhere. It remains to be seen, however, whether the FTC Report will have a substantive impact on how either of the follow-on biologics bills ultimately emerges from committee.

Edwards Angell Palmer & Dodge will continue to provide updates and analysis on this important topic. The firm has substantial experience in all of the areas that touch on the follow-on biologics debate – in particular, intellectual property litigation, life sciences, antitrust, and FDA regulatory practices.

¹ The FTC news release and links to the full report are available at <http://www.ftc.gov/opa/2009/06/biologics.shtm>.

² The FDA currently approves most applications for biologics via a Biologics Licensing Application (“BLA”), pursuant to the Public Health Services Act. There remain a few biologics, however, that are approved via the Food, Drug and Cosmetics Act and its more traditional New Drug Application (“NDA”) pathway. Neither of these routes, however, provides an *abbreviated* pathway for follow-on biologics, as currently exists for small-molecule drugs.

³ See H.R. 1427 (introduced March 11, 2009) and H.R. 1548 (introduced March 17, 2009). The companion bill to H.R. 1427 is S. 726, which was introduced by Senator Charles Schumer of New York.

⁴ The FTC Roundtable and related links are available at <http://www.ftc.gov/bc/workshops/hcbio/index.shtml>.

⁵ See, e.g., Jonathan D. Rockoff & Ron Winslow, *Merck to Develop Biotech Generics*, THE WALL STREET JOURNAL, December 10, 2008, at B1.

⁶ See, e.g., Jessica Dye, *Lawmakers Slam FTC Generic Biologic Report*, IP LAW 360, June 11, 2009. But see Chairman Waxman’s Statement on FTC Report on Follow-on Biologic Drug Competition, available at http://energycommerce.house.gov/index.php?option=com_content&view=article&id=1659:chairman-waxmans-statement-on-ftc-report-on-follow-on-biologic-drug-competition&catid=155:statements&Itemid=55.

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Kathleen B. Carr, Partner and Co-Chair,
Intellectual Property Litigation Group
Florence A. Crisp, Associate
Thomas H. Wintner, Associate

617.951.3326
401.276.6413
617.239.0881

kcarr@eapdlaw.com
fcrisp@eapdlaw.com
twintner@eapdlaw.com

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