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Federal Trade Commission
Office of the Secretary
600 Pennsylvania Avenue, N.W.
Room H-135 (Annex F)
Washington, DC 20580

VIA ELECTRONIC SUBMISSION

Emerging Health Care Competition and Consumer Issues - Comment, Project No. 083901

Dear Sir/Madam:

We submit these comments on behalf of Hospira, Inc. Hospira thanks the Federal Trade Commission for its interest in legislation to establish an abbreviated regulatory approval pathway for biosimilar drugs.

If you have any questions or require any additional information after reviewing these comments, please do not hesitate to ask. Hospira looks forward to continuing to work with the Commission and Congress on this critical issue.

Respectfully submitted,

Kelsey I. Nix

Enclosure

Emerging Health Care Competition and Consumer Issues - Comment, Project No. P083901

Comments From Willkie Farr & Gallagher LLP on Behalf of Hospira, Inc., Addressing Topics Raised In Connection With The FTC Roundtable Held November 21, 2008

For over 20 years, Hatch-Waxman has successfully balanced the interests of American consumers and the interests of reference and generic drug companies. That balance has delivered annual cost savings of $8-10 billion to patients and encouraged innovation with the introduction of over 4,500 new drugs.[1] Hatch-Waxman's time-tested balance and structure should be extended to biologics.

The extended data exclusivity ("DE") terms sought by reference drug companies (e.g., 14 years instead of Hatch-Waxman's five years) would retard innovation in a biologics industry already amply protected by patent rights.[2] Hatch-Waxman has demonstrated that competition drives innovation, not extended market exclusion.[3] In addition to retarding innovation, extended DE terms would also prolong monopoly prices and deprive consumers of estimated cost savings of $25-108 billion over the next decade alone.[4]

I. Biotechnology Patents Provide Strong Protection For Biologics

A. Product Patent Claims Protect Biologics

There is no reason to believe that biologics are any less patent protected than their chemical drug counterparts. Like chemical drugs, biologics are often protected by several patents. Patent portfolios for biologics and chemical drugs include the same basic types of patents: product, process, platform technology, and method of treatment. During the FTC's November 21, 2008 Roundtable, reference biologic company representatives urged that one of these patent types – product patents – have claims that are too narrow to protect against biosimilar competition. However, there is no evidence of a Patent Office bias against the biotechnology industry. Patent claims result from a negotiation between the Patent Office and the applicant in light of the prior art and the statutory requirements of written description, enablement, etc. The reference companies have the resources to afford highly skilled patent counsel to obtain the broadest claim coverage to which they are entitled.[5]

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[1] Senator Hatch confirmed Hatch-Waxman's success, commenting that it "it saves an estimated $8 to $10 billion for consumers each year." 149 CONG. REC. S16104, 16104 (daily ed. Dec. 9, 2003). *See* Laurence J. Kotlikoff, *Stimulating Innovation in the Biologics Industry: A Balanced Approach to Marketing Exclusivity* (September 2008), p. 13, Fig. 3 (hereinafter *Kotlikoff*).

[2] *See, e.g.*, BIO Comments, Response to Question A7; Amgen Comments, Response to Question A7; Pharmaceutical Research and Manufacturers of America (PhRMA) Comments, Response to Questions A7-8; and Wyeth Pharmaceuticals Comments, Response to Question A7.

[3] Kotlikoff, *supra* note 1, at 10, 11.

[4] *Id.* at 12.

[5] *See* Joseph A. DiMasi et al., *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, Manage. Deci. Econ., 28: 469-479, Abstract (2007) (estimating biologics development at $1.2 billion) (hereinafter *Is Biotech Different?*).

Biologic product claims have successfully prevented competitors from entering the market. In *Amgen, Inc. v. F. Hoffmann-La Roche Ltd.*,[6] for example, Amgen successfully asserted patent claims to an amino acid sequence for recombinant erythropoietin ("EPO") (a naturally occurring protein that stimulates the production of red blood cells). Amgen's product patent prevented competition from a pegylated-EPO product. The *Amgen* decision undercuts Amgen's own comment that "for some biotech products that are the recombinant version of a known naturally occurring product only limited patent protection, or none, may be available on the product itself."[7]

Hoffman-La Roche's accused biologic product was different in size and performed differently from Amgen's product. Accordingly, the *Amgen* case also rebuts the argument that FDA's approval of a biosimilar that is "similar" but not "the same as" the reference drug would strip the protective power of product patents.[8] *Amgen* also demonstrates that product claims covering only a portion of a biologic can block competition by similar biologics. Biologics are large molecules, and product patents typically claim only their "active" regions.[9] These active regions engage the molecule with its surrounding environment and create the therapeutic effect. Thus, while biosimilars might be similar, but not identical, their functionality will likely require resolution of product claims covering the biologic's active regions, regions that will often be shared by both the reference biologic and the biosimilar.

B. Process Patents Are More Important For Biologics

Hatch-Waxman does not require Orange Book disclosure of applicable process patents.[10] However, process patents are important to biologic drugs.[11] Even BIO, an organization promoting extended DE measures, agrees that "[c]laims to manufacturing processes are more important in biotechnology than they are in the small molecule [chemical] space."[12] That is because many process patents for making chemical drugs can be, and are often, circumvented. Processes for reliably producing biologics, however, can be difficult to establish in the first instance, making a patent to such a process more difficult to circumvent.[13] As BIO explained:

> The processes by which biologics are made are highly specific, complex, and *determine many of the biologic's functional and structural characteristics*, such as the way the

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[6] Civ. Action No. 05-12237, 2008 U.S. Dist. LEXIS 77343 (D. Mass. Oct. 2, 2008) (granting a permanent injunction).

[7] Amgen Comments, Response to Question A6.

[8] *See id.*

[9] We note that EPO is a small protein (165-166 amino acids) and that the product claims at issue in *Amgen* claim EPO's full amino acid sequence. However, full sequence product claims are not typical of larger proteins.

[10] 21 U.S.C. § 355(b)(1)(G) (2008).

[11] BIO Comments, Response to Question A6(e); Amgen Comments, Response to Question A6 ("Biotech product patent portfolios are more likely to include patents on the process for making the product than other types of product patent protection. . . . Biotech patent portfolios often contain certain kinds of patent claims – such as process claims and claims that confer indirect protection – that are less frequently seen in small molecule product patent portfolios."); Hospira, Inc. Comments, Response to Question A6(e); Amgen Comments, Response to Question A6.

[12] BIO Comments, Response to Question A6(e).

[13] *See id.*, Response to Question A1.

protein is folded; the presence and position of sugar or fatty acid side chains; the way proteins aggregate; the way both ends of the protein's amino acid chain are truncated or extended; the presence of protein isoforms in the final preparation, or its impurity profile, and the like. Such *product characteristics* can often be expected to affect the product's safety, purity, and efficacy profile, and thus *are integral to the approval of the product itself.* Thus, many important inventions are made as biologics manufacturers work out optimal processes to reliably and reproducibly make, purify, and process a biologic molecule.[14]

Reference drug companies are in the best position to know which patents cover their products. Accordingly, the biosimilars legislation should require reference companies to list their applicable process patents in a biologics Orange Book.[15] Proper notice of process patents would allow a biosimilar company to assess the intellectual property risks of product development and to determine whether it would be technically feasible to develop a different process.

C. Reference Companies Also Should Disclose Applicable "Submarine" And "Platform Technology" Patents

Biologics are also more likely than chemical drugs to be covered by "submarine" patents. The disclosures of submarine patents are not public before the patents issue. Submarine patents issue from original patent applications filed before November 29, 2000.[16] In addition, submarine patents that issue from original applications filed before June 8, 1995 carry a longer term (17 years from issuance, rather than 20 years from the application date).[17]

Because biotechnology companies filed multiple continuation and divisional applications based on older applications, many submarine patents likely are still pending. Hospira's representative at the FTC Roundtable stated that "in Hospira's experience, every single biopharmaceutical product that we have looked at, there are submarine patents in effect."[18] Eli Lilly's representative agreed, stating that as Hospira's representative "quite properly pointed out, there are patents issuing probably tomorrow that are probably pre-GATT [i.e., filed before June 8, 1995] that will have 17 years of life."[19] Amgen likewise acknowledged that "[f]or most biotech patent applications, the examination process by the Patent and Trademark Office (PTO) lasts much longer" and "biologic products are typically in late

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[14] *Id.*, Response to Question A6(e).

[15] *See* BIO Comments, Response to Question A6(e) ([L]egislation should contain adequate provisions to account for the importance of process patents in the biologics space, ..."). *See also* Amgen Comments, Response to Question B3 ("[D]ue to the potential of different types of biotech patents, a patent listing process such as the Orange Book regime used for small molecules would not capture all the relevant patents. . . .").

[16] *See* 35 U.S.C. § 154(c) (2008); Changes to Implement Eighteen-Month Publication of Patent Applications, 65 Fed. Reg. 57024 (Sept. 20, 2000).

[17] *Id.*

[18] Transcript of FTC Roundtable at 146, lines 22-24.

[19] *Id.* at 175, lines 11-13.

stage clinical trials, *or even on the market (some for several years), before the PTO issues the patent(s) that protect the product.*"[20]

To address this problem, biosimilars legislation should require both (1) disclosure of applicable submarine patent applications in a biologics Orange Book and (2) compulsory licensing of any undisclosed submarine patents that issue after a biosimilar is approved.

Biotechnology platform technology patents typically cover basic techniques such as using host cell and vector components, and methods of making humanized antibodies. Because of the biotechnology industry's relative youth (especially as compared to the chemical drug industry), early platform technology patents generally apply to many biologic drugs. Biosimilars legislation should require reference companies to identify applicable platform technology patents in a biologics Orange Book.

II. Hatch-Waxman Is The Correct Model For An Abbreviated Biologics Approval Pathway

A. Extended Data Exclusivity Terms Are Not Warranted

Adopting an improved Hatch-Waxman model for biologics would balance the interests of reference and biosimilar drug companies -- just as it has long balanced the interests of reference and generic chemical companies. However, adding years to Hatch-Waxman's DE terms, as the reference biologics industry urges, would unhinge that balance, unnecessarily prolong monopoly prices, and block competition by biosimilars.

The development costs for new biologic ($1.2 billion) and chemical drugs ($1.3 billion) are comparable.[21] However, development costs for biosimilars (tens of millions of dollars) are significantly greater than for generic chemical drugs (approximately $1-2 million).[22] In light of these greater development costs, even Hatch-Waxman's current DE terms might dissuade many companies from undertaking the development of biosimilars.

The rationale for DE terms is to compensate for time invested in waiting for FDA approval. Reference biologic companies seek to extend Hatch-Waxman's current four-year DE term (when an ANDA applicant files a paragraph IV certification) for new drugs to 14 years – a 350% increase.[23] Reference biologics take on average about 97.7 months to gain FDA approval; meanwhile, chemical drugs take 90.3 months.[24] Plainly, this 8% difference in FDA approval time does not justify upsetting Hatch-Waxman's balanced DE term provisions with a 350% increase.

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[20] Amgen Comments, Response to Question A6 (emphasis added).

[21] Is Biotech Different?, supra note 5, Abstract.

[22] Grabowski, Henry, et al., *The Effect on Federal Spending of Legislation Creating a Regulatory Framework for Follow-on Biologics: Key Issues and Assumptions*, White Paper, p. 26, 34, August 2007 (hereinafter *Federal Spending*).

[23] 21 U.S.C. § 355(j)(5)(F)(ii) (providing that an abbreviated application may be submitted after the expiration of four years from the reference drug's approval date if it contains a certification of patent invalidity or non-infringement).

[24] Is Biotech Different?, supra note 5, Fig. 2.

B. The Importance Of "Interchangeability"

Interchangeability is a key factor for consumers to derive the full economic benefit of biosimilars. Biosimilars legislation should authorize the FDA to establish appropriate standards for demonstrating "interchangeability."[25] Designation of a biosimilar as "interchangeable" will promote market penetration and maximize the enormous savings to consumers, estimated at $25-108 billion over the next decade.[26]

Without an "interchangeable" designation, biosimilar companies would be compelled to invest significant sums to market and promote biosimilars, thus driving up the cost to the consumer.[27] Reference companies also would have less incentive to compete on price. Reference drug companies would more likely try to out-market the biosimilar companies, further driving up the costs of *both* the reference drug and market entry by the biosimilar.

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Both the biologic and chemical drug industries involve large financial investments, long periods of FDA review, and strongly protective patent portfolios. These shared industry features are appropriately addressed by the market exclusivity and patent provisions of Hatch-Waxman. Differences between the biologic and chemical drug industries, where they do exist, weigh in favor of providing greater incentives to biosimilar companies to speed consumer access to biosimilars. Accordingly, the extended DE terms sought by several reference drug companies are not warranted. To ensure the continued success of Hatch-Waxman, biosimilars legislation also should require timely disclosure of all applicable patents and empower the FDA to establish biosimilar "interchangeability" standards.

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[25] *See* Momenta Comments, Response to Question A2.

[26] Kotlikoff, *supra* note 1, at 12. *See also* Barr Pharmaceuticals, Inc. Comments, Response to Questions A1 and A2 (estimating cost savings of $43.2 billion and $71 billion over the first 10 years).

[27] Coalition for a Competitive Pharmaceutical Market Comments (CompRx), Response to Question A2; Federal Spending, *supra* note 22, at 26, 34.