UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

Office of the Secretary

May 2, 2008

The Honorable Frank Pallone, Jr.
Chairman
Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives
316 Ford House Office Building
Washington, D.C. 20515-5115

Dear Chairman Pallone:

The Federal Trade Commission is pleased to respond to questions from the Subcommittee on Health concerning the creation of a pathway for Food and Drug Administration ("FDA") approval of generic biologics products, also known as "follow-on" biologics ("FOBs"). As the Subcommittee has stated, generic versions of biologic products have the potential to lower costs and provide access to life-saving medicines for millions of American consumers. These benefits are unlikely to be realized unless Congress passes legislation enabling an effective mechanism for enhanced competition in biologics products, balanced by an appropriate recognition of the interests in maintaining consumer safety and long-term incentives for innovation. We applaud the Committee's work on this important issue, which can provide significant benefits to consumers.

Unintended consequences, however, could severely limit or eliminate the benefits of any legislation. To avoid some of these pitfalls, legislation first should ensure that generic biologics do not create another opportunity for brand and generic companies to enter into anticompetitive patent settlements. Second, Congress should consider the risks and rationales of establishing a period of generic exclusivity in the context of biologics. Finally, to the degree Congress determines that exclusivities to branded or generic companies are beneficial, it should limit companies' ability to game those exclusivities at the expense of consumers by (1) disconnecting the FDA approval process for generic biologics from patent litigation, and (2) ensuring there is no opportunity for brands effectively to lengthen their exclusivities through insignificant changes to a branded biologic product or through excessive procedural delays.

In addressing these issues, the Commission's response focuses on the Subcommittee's Patents Question 2: "What lessons can we learn from the Hatch-Waxman Act, and apply

towards Congress's discussion about FOBs?"[1] The Commission has extensive experience in examining competition under the Hatch-Waxman Act. In addition to numerous investigations and enforcement actions involving the conduct of brand-name and generic small molecule drug manufacturers arising in the context of the Act,[2] the FTC conducted a detailed empirical study of experience during 1993-2001 under the Hatch-Waxman Act's procedures designed to facilitate entry of generic drugs.[3] The Commission examined, among other things, settlements of patent infringement litigation filed pursuant to the Act, the effects of the 180-day marketing exclusivity period available to generic firms, and the patent listing system and the statutory 30-month stay triggered by the initiation of patent litigation under the Act, in order to assess the extent to which certain provision of the Act were susceptible to strategies to delay consumer access to low-cost generic alternatives to brand name drugs. Congress relied on the study in fashioning legislative reform of certain aspects of the Hatch-Waxman Act.[4] Since 2004, FTC staff also has reviewed every drug company patent settlement filed pursuant to the congressional mandate in the 2003 reforms, and issued annual reports on the types of patent settlements being undertaken.[5]

Although it appears that competition under any generic biologics legislation is unlikely, at least initially, to be as robust as current small-molecule generic drug competition, the Commission believes the lessons learned from the experience under the Hatch-Waxman Act can help Congress as it considers legislation to govern approval of generic biologic products. In significant respects, the Hatch-Waxman Act has succeeded in promoting competition in the pharmaceutical industry. By expediting the market entry of generic drugs, the Act has brought lower prices for consumers and provided a spur to innovation by branded-drug makers. But experience has shown that the Hatch-Waxman Act has also been subject to abuse, as some companies have attempted to "game" the system, securing greater profits for themselves without providing a corresponding benefit to consumers. The Commission is relying on its experience with competition issues in the context of the Hatch-Waxman Act in providing these comments.

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[1] Patents Question 2. In so doing, the response touches on matters relevant to questions concerning the effects of interchangeability on competition in the marketplace (Interchangeability Question 6); the appropriate ways for a generic biologics statute to handle patent listing and litigation (Patents Questions 4 and 6); and the effect of modifications to approved products (Incentives/Exclusivity/Investment Question 3).

[2] Information on these enforcement actions is available at http://www.ftc.gov/bc/0608rxupdate.pdf.

[3] *See* Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* (July 2002), available at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf, ("Generic Drug Study").

[4] *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Title XI, Access to Affordable Pharmaceuticals, PL 108-173, 117 Stat. 2066 (Dec. 8, 2003) ("Medicare Modernization Act").

[5] The reports are available at http://www.ftc.gov/bc/healthcare/drug/index.htm.

I. *The Potential Consumer Benefits From an Abbreviated Approval Process for Generic Biologics*

The Commission's experience with competition under the Hatch-Waxman Act suggests that generic versions of biologic drug products have the potential to offer substantial consumer benefits. By enacting Hatch-Waxman, Congress enabled the introduction of safe, lower-cost generic drugs for millions of American consumers. One study estimated that consumers saved $8 to $10 billion at retail pharmacies in one year alone by purchasing generic drugs.[6] Biologics, in contrast, currently are among the most expensive drug products, and the market for biologics is growing. While competition from generic biologics is unlikely to duplicate generic competition under Hatch-Waxman, in part because of scientific differences between biologics and small molecule drugs, Congress should bear in mind these potential consumer savings in considering generic biologics legislation. Generic biologics legislation will be most likely to enhance price competition if it provides an abbreviated approval process and a mechanism for automatic substitution, *e.g.*, interchangeability between a generic and a brand.

Under the Hatch-Waxman Act, Congress sought to "make available more low cost generic drugs," while fully protecting legitimate patent claims.[7] The Act allows for accelerated FDA approval of a drug through an abbreviated process, upon showing, among other things, that the new drug is "bioequivalent" to an approved drug.[8] Under state substitution laws, pharmacists may automatically substitute prescriptions for a branded drug to a bioequivalent generic.

Before the Act, competition from lower-cost versions of brand name drugs was weak. In 1983, the year before the Act's enactment, only 35 percent of the top-selling drugs with expired patents had generic versions available.[9] Federal Trade Commission studies in the late 1970's and early 1980's also showed that, absent automatic state substitution, physicians had limited incentives to shift patients to lower-cost brands.[10]

Generic competition under Hatch-Waxman in contrast has had dramatic effects. Studies of the pharmaceutical industry indicate that the first generic competitor typically enters the

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[6] *See* Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, Summary* 31 (July 1998), *available at* <http://www.cbo.gov/showdoc.cfm?index=655&sequence=0> (hereinafter "CBO Study").

[7] H.R. Rep. No. 857, 98th Cong., 2nd Sess., Pt. 1 (1984), *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2661.

[8] 21 U.S.C. § 355(j).

[9] *See* CBO Study, *Summary*. This figure excludes antibiotics and drugs approved before 1962.

[10] Federal Trade Commission, *Generic Substitution and Prescription Drug Prices: Economic Effects of State Drug Product Selection Laws* 7 (1985); *see also* Federal Trade Commission, *Drug Product Selection* 7 (1979).

market at a price that is 70 to 80 percent of the brand-name counterpart.[11] Subsequent generic entrants compete to drive the price down even further. As a result, and as a result of the policies of public and private health plans and state substitution laws, generic sellers typically capture anywhere from 44 to 80 percent of branded sales within the first full year after launch of a lower-priced generic product.[12]

Biologics currently do not face this type of generic competition. Yet sales of biologics were $40.3 billion in 2006, which was about 15 percent of total U.S. prescription drug sales of nearly $275 billion.[13] The biologics market is also growing: sales of biologics increased 9 percent in 2007, compared to just over 3.8 percent growth for overall pharmaceutical sales.[14]

Scientific differences exist between biologics and traditional small molecule drugs such that it may not be desirable or possible to import key features of the Hatch-Waxman system directly into biologics. Biologics may be more sensitive than small-molecule pharmaceuticals to changes in the manufacturing process. For some biologics, scientific studies may show that patients are not likely to be able to safely switch back and forth between a branded and a generic product. The scientific and patient safety questions involved in this determination are beyond the expertise of the Commission.

To the extent that the scientific issues can be adequately resolved with due regard for patient safety, experience with competition under Hatch-Waxman shows that an effective abbreviated approval process for generic products, with less stringent requirements than those for a new drug approval, can enhance competition with branded drug products. This experience further shows that multiple generic entrants increase price competition; and that automatic substitution enhances price decreases and shifts in market share. Generic biologics legislation that provides an abbreviated approval pathway – with incentives for multiple entrants, and a mechanism for automatic substitution – is consequently more likely to reap consumer savings.

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[11] *See* CBO Study; *see generally* David Reiffen & Michael R. Ward, *Generic Drug Industry Dynamics*, 87 REVIEW OF ECON. & STAT. 37-79 (2005).

[12] *See* CBO Study, xiii.

[13] IMS Health Inc., Press Release, *IMS Reports U.S. Prescription Sales Jump 8.3 Percent in 2006, to $274.9 Billion* (March 8, 2007), *available at* http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_80415465,00.html.

[14] IMS Health Inc., Press Release, *IMS Health Reports U.S. Prescription Sales Grew 3.8 Percent in 2007, to $286.5 Billion* (March 12, 2008), *available at* http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_83470499,00.html.

II. *The Risk of Exclusion Payments to Forestall Generic Entry*

Despite these potential benefits, generic biologics legislation presents a substantial risk of creating a new arena for exclusion payment patent settlements. Exclusion payment settlements, which to date have occurred only in the Hatch-Waxman context, are settlements of patent litigation in which the brand-name drug firm pays its potential generic competitor to abandon the patent challenge and delay entering the market.[15] These agreements are made at the expense of consumers, whose access to lower-priced generic drugs is delayed, sometimes for many years. These settlements are becoming more prevalent and threaten the benefits of the Hatch-Waxman Act.

One of the key steps that Congress took in the Hatch-Waxman Act was to promote the rapid introduction of generic drugs by establishing special procedures to enable firms seeking approval of generic drugs to challenge invalid or narrow patents on branded drugs. Experience under Hatch-Waxman has shown that many drug patents, if challenged, will not stand in the way of generic entry, and that successful challenges can yield enormous benefits to consumers. In its Generic Drug Study, the Commission studied all patent litigation initiated from 1992 through 2000 between brand-name drug manufacturers and Paragraph IV generic challengers, and found that the generic prevailed in cases involving 73 percent of the challenged drug products.[16] Many of these successes involved blockbuster drugs and allowed generic competition, and the accompanying cost savings, years before patent expiration. For example, generic entry as a result of successful patent challenges to four drugs alone (Prozac, Zantac, Taxol, and Platinol) is estimated to save consumers over nine billion dollars.[17]

Exclusion payments settlements significantly reduce the possibility that consumers will receive the benefits of generic drug entry prior to patent expiration. The profit that the generic firm expects to earn by competing may be less than the profit the brand-name drug company stands to lose from the same sales. Therefore, it may be more profitable for both parties if the

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[15] These settlements can include both cash payments or other consideration flowing from the brand to the generic. For a recent example of an enforcement action concerning exclusion payments, *see Fed. Tr. Comm'n v. Cephalon, Inc.*, No. 1:08-CV-00244 (D.D.C. filed Feb. 13, 2008). For a more detailed discussion of exclusion payments, *see* Prepared Statement of the Federal Trade Commission Before the Subcommittee on Commerce, Trade, and Consumer Protection, Committee on Energy and Commerce, U.S. House of Representatives, on Protecting Consumer Access to Generic Drugs: The Benefits of a Legislative Solution to Anticompetitive Patent Settlements in the Pharmaceutical Industry, 10-12 (May 2, 2007), *available at* http://www.ftc.gov/os/testimony/P859910%20Protecting_Consume_%20Access_testimony.pdf, ("FTC May 2007 Testimony").

[16] Generic Drug Study, at 19-20.

[17] *Generic Pharmaceuticals Marketplace Access and Consumer Issues: Hearing Before the Senate Commerce Comm.*, 107th Cong. (Apr. 23, 2002) (statement of Kathleen D. Jaeger, President & CEO, Generic Pharmaceutical Ass'n) at 12, *available at* http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_senate_hearings&docid=f:79636.wais.

brand-name manufacturer pays the generic manufacturer to settle the patent dispute and the generic manufacturer agrees to defer entry. The parties eliminate the possibility of competition and a lower-priced generic, and share the resulting benefits. Recent court decisions have made it more difficult to bring antitrust cases to stop exclusion payment settlements, and while the Commission is continuing to pursue law enforcement, the agency believes that a legislative solution to the existing problem would be desirable.[18]

Patent challenges are likely to be important for promoting the availability of generic biologic drug products as well to ensure that the mere presence of a patent does not act as an unwarranted barrier to market entry. A pre-marketing patent litigation process can create consumer benefits by enabling generic biologic applicants to enter the market sooner than they otherwise would by allowing early resolution of patent litigation. But the consumer benefit in pre-entry litigation is not realized if the parties can collude and share the profits preserved by avoiding competition.

Accordingly, in any legislation on generic biologics Congress should seek to avoid creating a new arena for this costly type of collusion. Due regard for patent rights is important, for the development of new biologic drugs is risky and costly, and preserving incentives to undertake this task is critically important. But exclusion payment settlements achieve exclusion not by virtue of the strength of the patent, but instead by paying for the exclusion. Provisions of the sort contained in H.R. 1902 would prevent generic biologics legislation from fostering exclusion payment settlements. In addition, requirements that drug company agreements be filed with the antitrust agencies, similar to those in the Medicare Modernization Act, would enable the agencies and the Congress to monitor the nature of patent settlements involving generic biologic products.

III. *The Need for Caution in Creating a Marketing Exclusivity Period for Generic Applicants*

Congress should be cautious about creating a marketing exclusivity period for generic biologic drug applicants – such as an exclusivity to the first applicant to receive FDA approval to market a generic biologic as "interchangeable" with a branded product. This is so for two independent reasons. First, experience under the Hatch-Waxman system suggests that this type of exclusivity may be abused. There is a risk that awarding an exclusivity period to generic biologic applicants might promote opportunistic behavior that harms consumers without providing any corresponding benefits. Second, it is not evident that the rationale under Hatch-Waxman for providing such an exclusivity necessarily extends to generic biologics.

The Hatch-Waxman Act, as amended by the Medicare Modernization Act, provides a 180-day market exclusivity period to the first company that seeks FDA approval to market a

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[18] *See* FTC May 2007 Testimony, at 21-24.

generic product prior to the expiration of certain patents relating to the brand name drug. No other generic manufacturer may obtain FDA approval to market its product until the first generic has sold its product for 180 days, unless the later generic wins a patent challenge against the brand.[19] If the brand does not sue a later generic applicant, that generic is essentially blocked from receiving approval. In addition to limiting competition during the 180-day period itself, the exclusivity can create a "cork in the bottle" that blocks entry from *any* generic firm when the first filer refrains from entering the market.

As a result, branded drug firms have an incentive to encourage generic firms holding the 180-day exclusivity to delay entering the market to avoid any generic drug competition. They have done so first through exclusion payment settlements, which the 180-day exclusivity facilitates. They also have done so by settling their patent suits with first generic applicants holding the 180-day exclusivity without an exclusion payment, and then refusing to sue later generic applicants.[20] If Congress creates an exclusivity period for generic biologics companies, it should ensure that brand companies can not use that exclusivity– an incentive to promote generic entry – as a way to prevent generic entry.

In light of this risk of abuse, the rationale for a generic exclusivity period should be carefully weighed. One of the main rationales for the 180-day exclusivity in the Hatch-Waxman context was to provide an incentive for generic drug companies to bear the cost of patent litigation to challenge potentially invalid or narrow patents: challenges that, if successful, benefit other generic applicants who can more easily enter the market when the patent is invalidated or narrowly-construed. Without the exclusivity, any one generic manufacturer would have limited incentives to assume all the costs and risks of a patent challenge. The profits of the first generic to win patent litigation would be limited if its victory opened the market to other generic versions of the branded product. This rationale for the generic exclusivity in the Hatch-Waxman context may be absent in the framework of biologics legislation that, as discussed in greater detail below, disconnects the FDA approval process from patent disputes between branded and generic applicants.

It is important to consider whether there is a danger that other generic companies will "free-ride" on the work done by the first company to receive FDA approval to market a biologic product as interchangeable with a branded product. Data on whether the first company's work is likely to reduce the approval time and studies required for subsequent applicants would be valuable. Absent such a justification, it is not apparent that drug companies would need an

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[19] There are provisions for a company forfeiting the exclusivity period, which occur in very limited circumstances.

[20] *See* Brief of Amicus Curiae Federal Trade Commission Supporting Appellant and Urging Reversal, *Teva Pharmaceuticals USA, Inc. v. Pfizer, Inc.*, No. 04-1186 (Fed. Cir.) (March 31, 2004) (generally describing the "bottleneck" under the Hatch-Waxman / Medicare Modernization Act system and strategies to "park" the first exclusivity). Recent court decisions have the potential to eliminate the effectiveness of this strategy, but the extent to which they will do so is still unclear.

additional incentive, beyond the reward that the market provides, to seek approval to market interchangeable generic biologics products.

In addition, if legislation does not permit interchangeability between the products of later generic biologics applicants with those of the first generic applicant, the first generic applicant may not face the same extent of competition from other generic applicants as it does under the Hatch-Waxman system. In that case, the necessity of providing an exclusivity in these circumstances to a first generic applicant is even more questionable.

IV. *The Potential for "Gaming" to Lengthen Exclusivity Periods*

The Commission's experience under Hatch-Waxman teaches that any exclusivity periods provided to branded (or generic) biologics firms must be carefully designed to minimize gaming strategies that effectively lengthen these periods. Legislation should ensure that strategies employed under the Hatch-Waxman framework to restrict competition are not replicated in biologics. Such legislation also should avoid enabling new gaming strategies unique to the new provisions enacted.

Although the Hatch-Waxman Act has been largely successful, companies have found ways to frustrate some of the Act's goals. The following are examples of these strategies:

- *Multiple 30-month stays.* The Hatch-Waxman Act supplied a 30-month stay of FDA approval of a generic drug if a branded drug manufacturer sued a generic manufacturer for infringement of a patent that the brand "listed" with the FDA as covering its drug, and the generic applicant had issued a certification stating that it intended to challenge that patent.[21] Over time, branded manufacturers began successively to list multiple patents with the FDA. A number of these subsequently-listed patents were narrow or weak patents on minor aspects of the listed drug.[22] This strategy allowed the brand-name company to obtain additional 30-month stays delaying FDA approval of generic drugs. Congress ultimately remedied this problem in the Medicare Modernization Act by limiting branded drug companies to a single 30-month stay, but only after consumers lost substantial competition from generic drugs during the periods of these "stacked" 30-month stays.

- *"Switch" and elimination of substitution for the initial product.* Branded drug manufacturers have made minor, non-clinically significant changes to a branded product

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[21] *See* 21 U.S.C. § 355(j)(5)(B)(iii) (2002); *see also* 35 U.S.C. § 271(e)(2)(A) (2002). A single 30-month period approximated the time necessary for FDA review and approval of the small molecule generic drug application and the duration of a patent lawsuit. Generic Drug Study, at iv.

[22] Generic Drug Study, at 40.

that enable them to limit generic competition and obtain multiple exclusivity periods.[23]

- *Regulatory process.* Branded drug manufacturers have used procedures at the FDA to file "citizen petitions" with the FDA shortly before approval of a generic application. According to testimony by the FDA in 2006, "a high percentage of the petitions" are denied.[24] These petitions have the potential to delay generic drug approval. FTC staff have commented that abusing this process may be a lucrative strategy.[25]

The potential to "game" the system to effectively lengthen exclusivity periods is particularly pronounced when FDA approval of a potential generic entrant is tied to events in the patent litigation between the generic firm and the branded company. Tying exclusivity periods for biologic products to patent litigation creates the opportunity for gaming because the timing and scope of the litigation are substantially under the control of one or both of the litigants. Legislation that does not link the patent litigation process with FDA approval of generic biologics may help to reduce gaming by removing the incentives to skew the conduct of patent litigation to extend exclusivity periods.

Even if branded and generic exclusivity periods are not connected to the patent dispute resolution process, some opportunities for gaming and collusion may remain. Based on the FTC's experience under the Hatch-Waxman system, the more complicated the pre-marketing patent litigation system, the greater the chance that the system may be gamed or may result in competitive consequences unforeseen at the time the legislation is enacted. A system of pre-marketing patent litigation that is simple and transparent is less likely to result in competitive harm. Such a system could involve private exchange of patent information. It also could involve publication of relevant patents at the FDA or otherwise in a public forum, so long as the listing of the patents is for informational purposes and does not delay FDA approval of generic biologics products.

Regardless of any pre-marketing patent dispute resolution system, any biologics legislation should ensure that a branded biologics company may not obtain multiple lengthy exclusivity periods for minor, non-clinically significant changes to its products. The appropriate

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[23] *See Abbott Labs. v. Teva Pharm. USA, Inc.*, 432 F. Supp. 2d 408, 413 n.1 (D. Del. 2006) for an example of litigation alleging this type of strategy. *See also* Herbert Hovenkamp, Mark D. Janis & Mark A. Lemley, *IP and Antitrust*, § 12.5 (2006).

[24] Statement by Gary Buehler, R.Ph., Director of the Office of Generic Drugs, Center for Drug Evaluation and Research Food and Drug Administration, U.S. Department of Health and Human Services on Improving Access to Generic Drugs, Before Special Committee on Aging, United States Senate (July 20, 2006), *available at* http://www.hhs.gov/asl/testify/t060720.html.

[25] Generic Drug Study, at 66. The Commission found that a set of 12 citizen petitions filed and answered prior to 2003 did not affect the timing generic entry, but the Commission noted the potential for delay. *Id.* at 65, 67.

length of any exclusivity period for a branded manufacturer is a complicated policy judgment.[26] Congress should make that determination, and companies should not be able to lengthen it. Making the terms of an exclusivity well-defined and not subject to extension from insignificant changes to the branded biologics product is one way to limit this threat. It may be useful for generic biologics legislation explicitly to address what general categories of changes, if any, to a branded biologics product will permit a period of additional branded exclusivity and the length of any such exclusivity.

Finally, generic biologics legislation should be structured in way that minimizes potential for regulatory delays or abuse of regulatory process, while appropriately safeguarding patient safety. Procedures that supply lengthy notice-and-comment periods as a precondition to approval of generic or interchangeable biologics open the door for strategic delays. Where Congress determines expedited procedures for approval of generic biologics are consistent with ensuring safe products, those processes will benefit consumers; however, there seems to be no reason for generic biologic legislation to establish more onerous procedural requirements for generic biologics than are required for approval of branded biologic products.

V. *Conclusion*

The Commission appreciates the opportunity to comment to the Subcommittee on generic biologics issues, and urges the Subcommittee to continue to consider the competitive implications of generic biologics legislation. The Commission and its staff welcome any future questions from the Subcommittee related to this important issue for American consumers.

By the direction of the Commission.

C. Landis Plummer
Acting Secretary

cc: The Honorable Nathan Deal, Ranking Member
Subcommittee on Health

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[26] The appropriate length of any such marketing exclusivity (akin to the "new chemical entity" marketing exclusivity provided to branded pharmaceutical manufacturers under the Hatch-Waxman Act) is beyond the scope of the Commission's present comments.