



Federal Trade Commission

FOLLOW-ON BIOLOGIC DRUG COMPETITION:

A REPORT BY THE FEDERAL TRADE COMMISSION

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Remarks as prepared for delivery¹ to the
Health Industry Forum
“Federal Strategies for Promoting Affordable Biologics:
Enhancing Market Competition”

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I. INTRODUCTION

Thank you for your kind introduction, and for inviting me to participate in this conference. I am pleased to have the opportunity to provide an overview of the Commission's hot-off-the-presses report on follow-on biologic ("FOB") drug competition,² which I am sure has been "required reading" for everyone in this room over the last 26 hours or so.

Unfortunately, I was unable to join you for this morning's sessions. I could not be here because, as most of you probably know, you are not the only audience who wanted to hear about the report today. I literally just raced over here from the Hill, where I was testifying on the Commission's behalf, on the same exact topic, before the Subcommittee on Health of the House Committee on Energy and Commerce.³

A primary goal of the Commission's report is to examine how competition is likely to evolve in biologics markets – in particular, between pioneer biologics and FOBs. The report sets forth our findings regarding the competitive dynamics of FOBs. We expect that the report will trigger a great deal of discussion, and we look forward to engaging in that process. In addition, we certainly hope that our recommendations will inform the legislative debate. We had a very large audience at this morning's hearing, so I feel comfortable in speculating that our report has attracted their attention.

I do want to emphasize that the report does not address any specific bills. The Commission recognizes that legislators are balancing many worthy objectives, as they seek to craft an FOB solution that best protects the public interest. Each bill may weigh those objectives differently. The Commission has limited its recommendations to competition issues, which are our core area of expertise. We believe, of course, that this competition perspective is of critical importance in the FOB debate – which is why we are grateful that legislators continue to offer us a seat at the table.

I will begin with a spoiler, telling you what I believe to be the fundamental premise of the Commission's report: that competition between pioneer biologics and FOBs is likely to look much more like current competition between two or more branded drugs that treat the same medical condition, and less like current competition between branded and generic versions of a drug. In my remarks today, I will explain why the Commission reached this conclusion, and identify some implications for any legislation that seeks to create an abbreviated regulatory approval pathway for FOBs. To provide some context, I will also highlight a few key defining characteristics of the biologics marketplace, as identified in the report.

²FEDERAL TRADE COMMISSION, EMERGING HEALTH CARE ISSUES: FOLLOW-ON BIOLOGIC DRUG COMPETITION: A FEDERAL TRADE COMMISSION REPORT (June 2009) [hereinafter FOB REPORT], available at <http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf>; see also FTC News Release, *FTC Releases Report on "Follow-on Biologic Drug Competition"* (June 10, 2009), available at <http://www.ftc.gov/opa/2009/06/biologics.shtm>.

³*Emerging Health Care Issues: Follow-on Biologic Drug Competition, Hearing Before the Subcommittee on Health of the House Committee on Energy and Commerce*, 111th Congress (June 11, 2009), available at http://energycommerce.house.gov/index.php?option=com_content&view=article&id=1663:energy-and-commerce-subcommittee-hearing-on-biologic-drug-competition&catid=132:subcommittee-on-health&Itemid=72.

II. THE COMMISSION'S INVOLVEMENT IN THE FOB DEBATE

But before I launch into the report, and by way of background, I want to share a brief overview of the Commission's involvement in the FOB debate, leading up to the issuance of this report.

I first spoke publicly about biosimilars in June 2007.⁴ (I believe I was the first person from the FTC to do so.) My audience was a group of lawyers who specialize in issues at the intersection of antitrust and intellectual property. Back then, I predicted that biosimilars would become a "hot topic" – and I announced that I wanted to see the Commission get more involved in the debate.

I was up-front about my agenda. First, I wanted to ensure that the dialogue on FOBs would include a principled and rigorous analysis of competition dynamics, especially from the consumer perspective. Second, I wanted to ensure that the FTC would be an integral part of the dialogue, given our expertise in generic drug competition, as well as our excellent relationship with other regulatory agencies and legislators who focus on drug issues. My staff and I reiterated similar themes in several subsequent speeches; I'm sure many of you were in the audience for at least one of them.

In April 2008, the Chairman and Ranking Member of the House Subcommittee on Health sent a letter and multiple pages of questions to 35 organizations, to solicit their views on biosimilars and to inform the development of legislation.⁵ I was pleased that the Commission was included on the list of stakeholders. This outreach from the Hill provided an excellent mechanism for the Commission to share some of its expertise. Thanks to our talented staff, who had been tracking these issues for quite awhile, the Commission was poised to provide some preliminary thoughts.

We did so in a ten-page letter⁶ focused primarily on one specific question posed by the Subcommittee: "What lessons can we learn from the Hatch-Waxman Act, and apply towards Congress's discussion about [follow-on biologics]?" Our letter endorsed the concept of an abbreviated approval process for FOBs. The letter also urged Congress to take care to avoid "unintended consequences" that might severely limit or eliminate the procompetitive benefits of biosimilars legislation.

⁴Pamela Jones Harbour, Commissioner, Federal Trade Commission, The Competitive Implications of Generic Biologics, Remarks at the Intellectual Property Antitrust Conference of the Sections of Antitrust and Intellectual Property Law, American Bar Association (June 14, 2007), *available at* <http://www.ftc.gov/speeches/harbour/070614genbio.pdf>.

⁵Letter from Frank Pallone, Jr., Chairman, & Nathan Deal, Ranking Member, Subcommittee on Health, Committee on Energy & Commerce, U.S. House of Representatives, to 35 groups (including Federal Trade Commission) (Apr. 3, 2008), *available at* http://energycommerce.house.gov/Press_110/110-ltr.040308.list.Biologic%20ltr.pdf.

⁶Letter from C. Landis Plummer, Acting Secretary, by direction of the Federal Trade Commission, to Frank Pallone, Jr., Chairman, Subcommittee on Health, Committee on Energy & Commerce, U.S. House of Representatives (May 2, 2008), *available at* http://energycommerce.house.gov/Press_110/110-ltr.050208.respto040308.FTC.pdf.

Research and scholarship are an important part of the Commission's mission. And so, a few weeks after submitting our letter to the House Subcommittee, the Commission published a Federal Register notice to solicit public comments and to announce its November 2008 public workshop on FOB competition issues.⁷

Given my history with FOB issues over the last couple of years, I must admit, I am quite gratified that the Commission has become so involved in the FOB discussion. Even more gratifying, competition dynamics have become a central focus of that discussion. I thank our talented FTC staff for their efforts in getting us to this point. From a procedural perspective, I view it as a victory for Commission advocacy whenever competition issues rise to the top of the agenda, because I believe so fervently that competition is one of the best ways to protect the interests of American consumers.

III. KEY CHARACTERISTICS OF THE BIOLOGICS MARKETPLACE

Let me now set the stage for a discussion of the Commission's substantive conclusions regarding the future of FOB competition. I will highlight some important characteristics of the biologics marketplace, as they are outlined in the report itself.⁸ These characteristics will be familiar to this audience – steeped, as you are, in the FOB debate. But I thought you might find it illuminating to see which facts we antitrust lawyers pluck out as relevant to our competition analysis.

We start from the most basic of facts: as you know, the emergence of biologic drugs has dramatically improved the lives of thousands of Americans over the past few decades. These therapies offer improved treatment options and quality of life, and reduce suffering. Often, they save lives. Biologics reflect some of the best of what modern science and technology contribute to our civilization.

These benefits, however, come at a huge cost. Unlike traditional “small molecule” drugs, biologics cannot be chemically synthesized in a laboratory. Biologics are “large molecule” protein-based drugs, derived from living cells, often through complex and expensive recombinant DNA processes. They are manufactured in sophisticated production facilities, and they reflect extensive investments in research and development.

Biologics, therefore, are expensive treatment options. I'm sure each of you has your own set of facts and figures on the tip of your tongue. Here are two examples I shared with the House Subcommittee this morning, taken from the report. The biologic Herceptin is used to treat breast cancer, and an annual course of treatment costs about \$48,000. Annual treatment for rheumatoid arthritis with Remicade, another biologic, can cost approximately \$20,000.

⁷FTC News Release, *FTC Announces Workshop and Roundtable on Emerging Health Care Competition and Consumer Protection Issues* (Aug. 27, 2008); Fed. Trade Comm'n, Public Workshops and Roundtables: Emerging Health Care Competition and Consumer Issues, Notice of Public Workshops and Roundtables and Opportunity for Comment, 73 Fed. Reg. 51479 (Sept. 3, 2008), both available at <http://www.ftc.gov/opa/2008/08/hcissues.shtm>.

⁸The remainder of these remarks closely track the FOB REPORT, *supra* note 2. Reference is made to citations included within the report itself.

As we all know, one way to reduce the costs of biologics would be to authorize the Food and Drug Administration (“FDA”) to permit follow-on biologics, or FOBs, to enter the market once a biologic drug’s patents expire. Currently, an FOB applicant must replicate all of the tests to generate a complete set of data about a biologic drug’s safety and efficacy, even where some of the prior knowledge about the pioneer biologic would also be relevant to the FOB. There is no statutory or regulatory pathway to allow abbreviated FOB entry without the FOB applicant having to duplicate the existing knowledge. This duplication represents an inefficient use of limited research and development (“R&D”) resources.

Also, as the FDA has explained, repeating all of the clinical trials raises ethical concerns associated with unnecessary human testing. Of course, these ethics issues are far beyond the scope of the Commission’s competition concerns, so I mention them only in passing. But I must admit, as a government official charged with protecting the public interest, I cannot help but think about the human costs of subjecting very sick patients to unnecessary double-blind studies, where some patients inevitably will receive placebos, even when we know for a fact that these patients are being denied safe and effective treatments.

Elements of the Hatch-Waxman Act provide a model for reducing FOB entry costs and addressing ethical concerns. Hatch-Waxman – which applies to small-molecule generic drugs – does not require generic applicants to duplicate the clinical testing of branded drugs that already have been proven safe and effective. By reducing R&D costs, Hatch-Waxman enables generic firms to enter the market with lower-cost versions of branded drugs.

Hatch-Waxman has successfully reduced drug prices, broadened access, and hastened the pace of innovation. But in other important respects, the Hatch-Waxman model is not a perfect template for FOB legislation. According to the FDA, there are key scientific differences between biologic and small-molecule drug products. Most notably, under Hatch-Waxman, in asking the FDA to rely on existing safety and efficacy data, the generic applicant must show that its product is “bioequivalent” to the branded drug product. This has at least three important implications.

- First, a bioequivalence showing is much less expensive to achieve, compared to the full clinical testing required for approval of a pioneer branded drug product.
- Second, if the generic drug is deemed bioequivalent to the branded drug, it usually can be safely substituted for the branded drug, and will be as effective as the branded drug. This means that the branded and generic can, in theory, compete head-to-head in the marketplace.
- Third, because such substitution is possible, many states have laws that allow pharmacists to *automatically* substitute a generic for a branded drug, unless a doctor has indicated otherwise. This substitution mechanism ensures that the generic will gain market share at the brand’s expense.

In stark contrast, biologic products cannot be perfectly duplicated – at least not based on current science and technology. Biologic products are so complex that even minor differences can trigger dangerous immune responses in a patient’s body. Technology is not yet robust enough to

determine whether an FOB product is “interchangeable” with the pioneer product. Due to the high risk of adverse effects, patients cannot switch freely between a pioneer biologic and an FOB.

Current FOB legislative proposals reflect the complexities of biologics. They would permit FDA approval of an FOB drug that is *similar* to, but not an exact replica of, the pioneer biologic product. Under these proposals, the FDA could rely on its previous findings regarding the pioneer biologic drug’s safety and efficacy, to the extent those findings also would be relevant to the FOB. An FOB manufacturer likely would save on some clinical testing expenses, which would reduce entry costs. But the savings would not be nearly as great as if only a bioequivalence showing were required. Also, the savings likely would vary depending upon the complexity of the pioneer biologic drug.

IV. THE COMMISSION’S STUDY OBJECTIVES

With that background in mind, let me turn to the Commission’s report. The purpose of our study was to evaluate how FOB competition is likely to develop and evolve, paying particularly close attention to the differences between small-molecule and biologic drugs.

The study was coordinated by an interdisciplinary FTC team that included not only pharmaceutical industry experts and competition policy specialists, but also patent lawyers and economists. I note this because the Commission is particularly proud of the breadth and talent of our expert in-house staff. In my view, whenever the Commission marshals these resources toward a common objective – such as in holding workshops and drafting reports – the results tend to be of very high quality. Even if you disagree with the FOB report’s conclusions, I hope you will agree that the report represents high-caliber work.

As I mentioned earlier, as part of its inquiry, the Commission solicited two rounds of public comments, which attracted submissions from approximately 30 industry participants and other stakeholders. In November 2008, the Commission conducted a public roundtable discussion that included over 30 panelists. The Commission also has examined European markets where FOB entry has occurred.

Our inquiry has been guided by an overarching question: whether competition between a pioneer biologic and an FOB is likely to be similar to competition between a branded and generic small-molecule drug. The Hatch-Waxman Act included specific provisions that were tailored to the unique competitive dynamics of generic drug markets. It is the Commission’s position that FOB legislation, likewise, should account for the unique competitive dynamics of FOB markets.

V. THE COMMISSION’S FINDINGS REGARDING FOB COMPETITION

As the report details, the Commission found that FOB competition is unlikely to be similar to generic drug competition. Rather, competition between a pioneer biologic and an FOB will look much more like competition between two branded small-molecule drugs.

In the interest of time, let me briefly summarize the four major reasons why FOB competition will not be like generic drug competition.

A. Entry Costs and Time

First is the extraordinary cost and time necessary to develop an FOB, which will sharply limit the number of competitors who can afford to enter, and also will limit the discounts the FOB can offer in relation to the pioneer price.

FOB products are likely to take eight to ten years to develop, and their development likely will cost between \$100 and \$200 million each. In contrast, small-molecule generic drugs typically take three to five years to develop, with product development costs of between \$1 and \$5 million. In addition, it is expected to cost between \$250 million to \$1 billion to build a new biologic manufacturing plant.

B. Pioneer Will Retain Significant Market Share

Second, follow-on entry will not radically erode the pioneer's market share. In the small-molecule space, when lower-cost interchangeable generics enter, the branded firm soon loses most of its share as patients switch to generics. But in biologics, a pioneer is likely to retain significant market share after FOB entry, largely due to the pioneer's first-mover advantage, the lack of interchangeability, no automatic substitution, and a smaller price discount.

In addition, doctors and patients may be reluctant to switch current patients to an FOB due to safety and efficacy concerns, which may limit FOB market opportunities to newly diagnosed patients.

C. Specialty Pharmaceutical Characteristics

Third, the specialty pharmaceutical characteristics of FOBs are likely to further constrain the FOB entrant's ability to gain market share. Specialty drugs are primarily injected or infused, and they are combined with ancillary medical services and products that require specialized training for proper handling and administration. These factors will make it more difficult to switch from a pioneer to an FOB alternative.

D. Payment Issues

Finally, because biologics are provided in clinic-type settings as part of medical treatments, they are not purchased and reimbursed in the same manner as small-molecule drugs. Payors cannot employ the same strategies, such as co-pays and tiered formularies, that empower consumers to seek generic drugs.

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As a result of all of these factors, the Commission's report predicts that FOB markets are likely to develop with the following characteristics.

- FOB entry is likely to occur only in biologic drug markets with more than \$250 million in annual sales.
- Only two or three FOB manufacturers are likely to attempt entry in competition with a particular pioneer drug product.
- These FOB entrants likely will not offer price discounts larger than 10 to 30 percent off the pioneer product's price. Although this discount is not as steep as with small-molecule generic drugs, it does represent millions of dollars in consumer savings for these very expensive products.
- Pioneer manufacturers are expected to respond by offering competitive discounts to maintain their market share. This price competition likely will increase consumer access and further expand the market.
- Without automatic substitution, FOB market share acquisition will be slowed. Pioneer manufacturers likely will retain 70 to 90 percent of their market share. This means that a pioneer firm will continue to reap substantial profits for years, even after entry by an FOB.

FOB market dynamics will contrast sharply with the market dynamics of generic drug competition, where lower-cost generic entry plus automatic substitution lead to rapid erosion of the branded drug's market share. When the first generic drug enters the market, it generally offers a 25 percent discount off the branded drug's price. As additional generic firms enter – and often there are eight or more of them – the price discounts reach as high as 80 percent.

In sum, FOB competition is likely to look much more like branded competition than generic competition.

VI. INCENTIVES THAT SUPPORT INNOVATION AND COMPETITION: PATENT PROTECTION PLUS MARKET-BASED PRICING

Given these likely dynamics of FOB markets, the Commission next asked whether any additional incentives will be needed to encourage FOB competition and foster ongoing biologics innovation. The report concludes that existing incentives – the same ones that motivate branded biologics – are sufficient. These two incentives are patent protection and market-based pricing.

Through patent protection and the resulting exclusionary rights, biotech firms increase their expected profits from investments in R&D. Patents thus foster innovation that would not otherwise occur.

Market-based pricing allows firms to charge prices that reflect the value of the drugs to consumers. By pricing at market rates, firms can recoup their substantial investments in biologic

drugs. Prices also enable firms to receive accurate market signals about the value of developing particular biologic drugs.

Currently, pioneer drug manufacturers race against other firms to bring products to market, in both pharmaceuticals and biologics. This competition benefits consumers by accelerating the pace of innovation, and also through eventual price competition. Given that FOB competition is likely to resemble competition by another brand, FOB competition is likely to promote the same consumer benefits, without the need for any additional incentives.

VII. IMPLICATIONS FOR FOB SYSTEM DESIGN

These findings have several implications for the design of an abbreviated approval system for FOBs. In the interest of time, I will briefly summarize what I view as the three key implications. I strongly encourage you to review the report itself for many more details.

A. Pioneers Do Not Need Additional Incentives to Innovate

First, pioneer manufacturers are unlikely to need additional incentives to continue to innovate in the face of FOB entry, beyond existing patent protection and market-based pricing.

It appears that pioneer biologics are capable of being covered by numerous and varied patents, including manufacturing and technology platform patents. There is no evidence that patents claiming a biologic drug product have been, or are likely to be, designed around more frequently than those claiming small-molecule products.

Market-based pricing – especially during the period of exclusivity granted by the patent system itself – provides strong incentives to innovate.

In light of these existing patent incentives, the Commission's report concludes that no additional period of branded exclusivity is needed to spur the development of new drug products, and that such exclusivity would actually be inefficient.

But an exception certainly could be made in situations where a drug molecule is in the public domain and therefore is not patentable. An exception also might be made in situations where market-based pricing provides insufficient incentives, such as in therapies for children or small patient populations.

B. Special Patent Resolution Procedures Are Unnecessary

A second implication is that it is unnecessary to implement special procedures to resolve patent issues between pioneer and FOB drug manufacturers.

The Hatch-Waxman procedures to trigger an early start of patent litigation made sense in the generic drug context, where there was a concern that generics would not be able to pay post-entry

patent infringement damages. But looking at the cost and complexity of bringing FOBs to market, it is likely that only well-funded firms will seek FOB entry, which will mitigate concerns about the enforceability of patent infringement judgments.

Special procedures are unlikely to succeed in raising and resolving all pertinent patent issues prior to FDA approval, especially given that pioneer biologics are covered by more and varied patents than small-molecule drugs. Special procedures also may create competitive problems – including, but not limited to, the “pay for delay” settlements we have seen in the Hatch-Waxman context.

C. FOB Manufacturers Do Not Need Additional Incentives to Develop Interchangeable Products

Third, FOB drug manufacturers are unlikely to need additional incentives to develop interchangeable FOB products, such as a marketing exclusivity period for the first FOB. A branded manufacturer does not receive any protection against market entry by another branded product. If FOB competition will closely resemble brand-to-brand competition, then the incentives provided by market-based pricing should be sufficient, and there is no reason to risk delaying the entry of subsequent FOBs that are ready for market.

VIII. A NOTE ABOUT THE NATURE MODEL

Knowing that Drs. Grabowski and Brill will be speaking on the panel right after my remarks, I do want to say just a few words about Appendix A of the Report. This Appendix describes and critiques the model that Dr. Grabowski first put forth in his *Nature Reviews* article last June.⁹ This model has been used as a basis to estimate the optimal length of a branded exclusivity period.

As you now realize, the report concludes that *no* branded exclusivity period is needed to promote competition and innovation, beyond the exclusivity already provided by the patent system. But given that current legislative proposals include exclusivity periods of varying lengths, the Commission felt it was necessary to identify some of the methodological and conceptual weaknesses of the model, which may lead to imprecise results.

I am not an economist, so I refer you to the Appendix itself for a detailed discussion and analysis. If you have questions, I know our staff would be happy to discuss them with you.

⁹Henry Grabowski, *Follow-on Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479 (June 2008). Subsequent calculations and adjustments to the Nature model include: Henry Grabowski *et al.*, *Updating Prior Analyses and Responding to Critiques*, DUKE UNIV. DEPT. ECON. WORKING PAPER, No. 2008-10 (Dec. 22, 2008); Matrix Global Advisors Comment (12/22/08); Alex Brill, *Proper Duration of Data Exclusivity for Generic Biologics: A Critique*, MATRIX GLOBAL ADVISORS, LLC, WHITE PAPER (2008).

IX. CONCLUSION

A couple of months ago, when staff first previewed the direction the report would be taking, one staffer joked with me: if each of the different constituencies will strongly disagree with something in the report, we are probably doing something right. Depending on the tone of your questions, we will see how that theory plays out.

I do thank you again for this opportunity to summarize the Commission's report, and I look forward to the panel discussion.