September 30, 2008

Federal Trade Commission
600 Pennsylvania Ave, NW
Washington, DC 20580

Re: Emerging Health Care Competition and Consumer Issues –
Comment, Project No. P083901

Federal Trade Commission:

Thank you for the opportunity to submit comments regarding a pathway for the Food and Drug Administration to approve generic biologics.

In drafting the attached responses, the member organizations of the Coalition for a Competitive Pharmaceutical Market (CCPM) relied upon the expertise within their given organizations. If you have any questions regarding our answers or require additional information, please do not hesitate to contact me.

On behalf of CCPM, thank you for your interest and attention to this important subject.

Sincerely,

Annette Guarisco
Chairman
Coalition for a Competitive Pharmaceutical Market

Coalition for a Competitive Pharmaceutical Market

Written Comments for Emerging Health Care Competition and Consumer Issues – Comment, Project No. P083901

Regulatory Exclusivities and Follow-On Biologic Drugs

1. What is the likely competitive effect of the market entry of a follow-on biologic competitor? Are there empirical models that predict the nature of this competition based on existing biologic drug product competition? How has competition developed between referenced and follow-on products in European markets? Would referenced product manufacturers lower their prices, offer discounts, and/or engage in enhanced marketing activities?

Response: We fully expect that the introduction of generic biologics within a therapeutic category would increase competition in that category and reduce overall spend within that category. This is especially the case for generic biologics deemed interchangeable. The impact on cost will be linked to the number of generic biologics introduced, the extent to which the generic is interchangeable, and the number of branded products that are already on the market.

In terms of how competition has developed between referenced and follow-on proteins in European markets, erythropoietin (EPO) can serve as an example, to the extent the EU provides a valid comparator to the U.S. To date, two generic biologic EPO molecules have been approved under five different marketing authorizations. While the approvals have been for the entire European Union, Germany presents the best case to date as a country experiencing significant competition upon the entrance of generic biologics to the market. This is largely due to the fact that companies have to receive pricing and reimbursement approval in each individual country in the EU, which is a lengthy process.

In Germany, the generic biologic products are starting to make an impact, as IMS data shows, almost 16 percent of first generation EPO sales are attributed to generic biologics (on a dollar basis), and nine percent of total EPO sales (including the second generation products). The best estimate is that the generic EPOs appear to be priced approx 25 - 30 percent below where the innovator price was prior to the entry of any generic biologic.

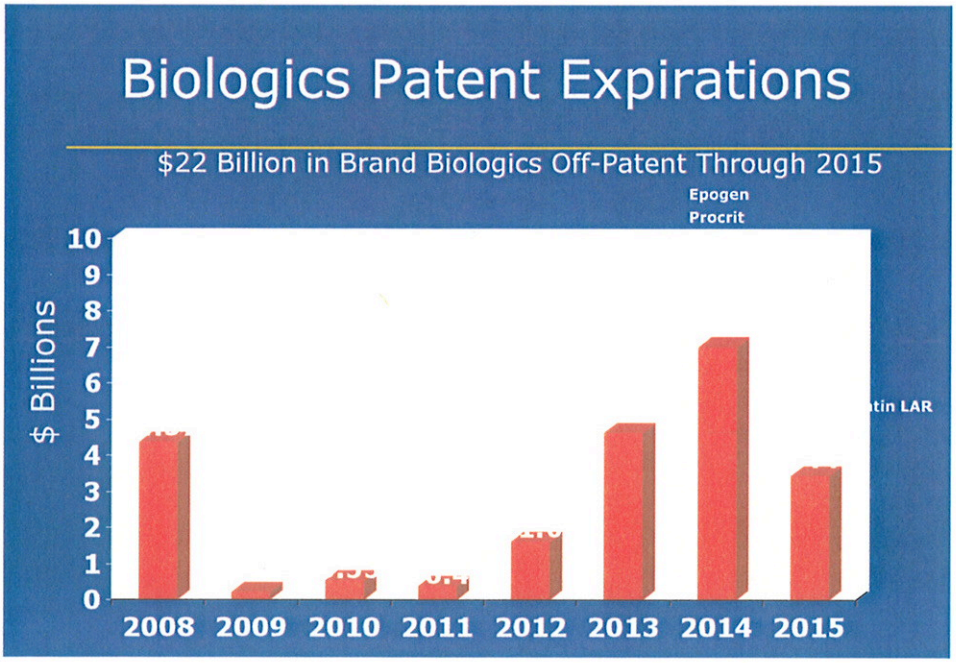
The following, which is also responsive to your question, was submitted by CCPM to the House Energy and Commerce Committee on May 2,2008:

> *Response -- Multiple savings estimates have been released over the last eighteen months. Express Scripts analysis considered four therapeutic areas across the entire market and concluded there was a ten year $71 billion dollar savings opportunity. Avalere Health released a ten-year forecast on savings to the federal government of $3.6 billion. Engel and Novitt forcasts a ten-year savings to the Medicare Part B program of $14 billion.*

While each study considered different populations and employed different assumptions about adoption, each study concluded that there is a multi-billion dollar savings opportunity. Actual savings may far exceed these forecasts, as we have seen higher than forecast listed discounts on Omnitrope. According to the March, 2008, edition of the Red Book, Omnitrope's price is a 34% discount from the original product. PBMs and group purchasers will reasonably expect much higher discounts.

The provisions of the final legislation will influence any savings estimates, such as requirements for interchangeability, any brand exclusivity awarded and how patent disputes are resolved, just to name a few. Also, the number of companies that submit applications for a follow-on product, whether a product or group of products is deemed interchangeable, how the follow-on companies decide to price their products, the acceptance rate for the follow-on agent in the marketplace, etc. will all be important factors in the savings equation.

The slide below (Medco, 2008) shows the biologics that already have or will lose patent protection by 2015. The estimated total 2007 US sales of all these biologics is about $22 billion. Some of these drugs are smaller and less complex proteins, while others are highly complex and will be more complicated to replicate. Not all of these products will receive a determination as interchangeable at the beginning.



However, assuming an 8% rate of price and utilization increase in each year from 2008 to 2015, the sales of the drugs in the chart above could approach $40 billion by 2015. In the following year, 2016, assuming all of these product have at least one follow-on versions approved, the savings could be projected by assuming an average AWP discount of 40% for the follow-on versions and a marketplace acceptance rate of 40%, as well. These average discounts and average market acceptance rate take into account that not all of the follow-on versions would be interchangeable with the reference product, and there may not be more than one follow-on version for some of these biologics. This would

yield an expected savings of $6.4 billion in 2016. Clearly, in the years prior to 2016 the savings would be less as patents may preclude FOBs for some of these biologics, and savings would be greater in subsequent years as additional biologics are subject to follow-on competition and marketplace of FOBs acceptance improves. Thus, in the 10 year period between 2011 and 2021, total savings could be in the range of $60 to $70 billion.

2. What is the likely impact of a follow-on biologic product being designated "interchangeable" (i.e., receiving an approval that would permit pharmacists, without physician authorization, to fill a prescription for the referenced product with the follow-on product)? What are the prospects for the use of "authorized follow-on biologics" in these circumstances? Do the answers to these questions differ based on the type of biologic product involved?

Response: If the generic biologic is not designated as interchangeable, the practical result will be that the product will be viewed as a lower cost, similar "brand" product that the generic manufacturers would need to significantly market. In the absence of a designation as interchangeable, it likely will take longer for the generic biologics to garner significant market share and brand manufacturers will have less incentive to compete based on price. They will more likely try to out-market the generic biologic.

If the generic biologic is designated interchangeable, the effect will be a more rapid infiltration into the brand market share. Because no interchangeable generic biologic products are available today, there is no historical experience to reliably predict how swift and to what degree this shift would occur. However, in the case of non-biologics, products deemed interchangeable achieve upwards of a 90-95% substitution rate in as little as one month following introduction. This creates enormous cost savings for the payor and the patient through lower co-pays and/or deductibles. As more interchangeable products are introduced, the obvious competitive nature creates even greater cost savings in the traditional drug space, as noted above.

3. What competitive concerns are raised by joint research and development, supply, licensing, marketing, and distribution agreements between referenced biologic manufacturers and their follow-on biologic competitors? What would be the likely impact of a requirement that agreements between referenced drug product manufacturers and follow-on biologic applicants be filed with the FTC and the Department of Justice Antitrust Division?

Response: As the FTC is aware, the Medicare Modernization Act of 2003 ("MMA") includes a provision requiring agreements between brand and generic companies be reported to both the FTC and DOJ, which allows these agencies to review the terms of such agreements. Expanding the MMA reporting requirements to cover generic biologics would be a logical step for Congress to take.

4. How would the prospect of competition from follow-on biologic drugs influence research and development for new biologic drugs, improvements to existing biologic drugs, and the timing and rollout of new and/or improved biologic drugs? Does the market experience with non-biologic generic pharmaceutical drug products provide insights into these issues?

Response: A science-based, generic biologics pathway would strengthen U.S. economic competitiveness by permitting low cost biologic medicines to reach patients in a timely manner. The pathway will reduce the cost of these medicines for patients and taxpayers as well as for individual businesses, resulting in billions of dollars of savings per year. By allowing businesses in all economic sectors to save on otherwise monopolistic biologic medicine prices, the pathway will enable those savings to be used to make U.S. businesses more innovative and competitive worldwide through such things as greater investment in research and development as well as heightened capital investments. The pathway will not affect valid and enforceable patent rights in any way, as can be seen with our experience with Hatch-Waxman. Clearly, there is no evidence that a lengthy exclusivity period or, at least one longer than provided for under Hatch-Waxman, is necessary to stimulate research and development. On the contrary, the research and development under Hatch-Waxman has lead to robust brand and generic marketplaces. (See response to #7 below.)

Hatch-Waxman created a science-based generic approval pathway with fair incentives for innovators to continue to innovate. That formula has had a positive effect on research and clinical programs throughout the U.S. There is no reason to believe a generic biologic approval pathway would have any less positive effects in the biologics arena if adopted in the mold of Hatch-Waxman. On the other hand, a pathway with unnecessary obstacles to generic approval or unduly long market exclusivity periods for branded biologics would lead to less innovation and no incentive to compete in the biologics arena.

5. How does the method used by Medicare for reimbursement of biologic drug products affect pricing and competition of referenced biologic products? What factors are important for this effect and why? How would the Medicare reimbursement system likely affect prices for both the referenced and follow-on biologic products? For example, does Medicare reimburse Part B drugs, including biological drugs, based on the Average Sales Price of all the biological drugs whose National Drug Codes (NDCs) reference the same Biologic License Application (BLA)? If so, how would a follow-on biologic drug that does not reference the BLA of the referenced drug affect the Medicare reimbursed price for referenced drug product? How will these and other Medicare reimbursement methodologies likely affect models of price competition after follow-on biologic drug entry?

Response: The most important factor to spur provider and beneficiary adoption of generic biologic products is that generic biologics share the same International Nonproprietary Name (INN) with the reference product. Hatch-Waxman allowed generic products to share the same name as reference products, which is an important element to the pathway

being considered.

We also encourage the Medicare program to use beneficiary cost sharing as a means to encourage the utilization of generic biologic products. Tiered co-payments and other cost sharing structures based on drug costs are an effective way to encourage utilization of generic biologics and other lower cost therapies.

6. How are the patent portfolios claiming biologic drugs similar or dissimilar to the patent portfolios that claim small molecule (nonbiologic) drugs approved under the federal Food, Drug, and Cosmetic Act (FDCA)?

Response: Brand biologic drug products are protected by patent portfolios (often extensive portfolios), just like their branded traditional small molecule counterparts. The ways in which brand companies patent biologics drugs might be different in some respects from traditional molecule patents, but biological drug products enjoy the same broad scope of patent protection enjoyed by traditional small molecule drugs when those drug products have novel and innovative aspects to them. This is why biologic patents have been successfully asserted in various disputes that have been, and continue to be, litigated in the courts. It is reasonable to assume that innovators would defend their patent rights against generic biologics as ardently than they do today against chemical generic applicants.

7. Are the regulatory exclusivities currently provided to pharmaceutical drug products in the FDCA appropriate for new biologic drugs and/or significant improvements to existing biologic products? Are they appropriate for specific types of biologics? Why or why not?

Response: Based on published analysis, it has been reported that the R&D costs for traditional and biopharmaceutical drugs are almost identical ($1.2 billion versus 1.3 billion). Therefore, there appears to be little financial argument for a lengthy period of exclusivity for biopharmaceutical products based on R&D costs.[1]

Product exclusivities are one of the mechanisms to reward innovation, and are intended to be linked to the importance of the product to society. An argument has been made that biologic drugs are more innovative and provide greater benefit to society, and therefore merit a longer period of exclusivity. However, the facts do not support this contention. For example, in the treatment of renal cell carcinoma, alfa interferon, a biologic, has long been a standard therapy. The recent introduction of small molecule drugs like Sutent and Nexava have provided a better treatment alternative for patients with this condition. These small molecules get only the standard 3-year exclusivity, even though they are better than the large molecule protein for this condition.

Gleevec, another small molecule drug that gets 3 years exclusivity, has revolutionized treatment of chronic myelogenous leukemia (CML) in a way that few biotech drugs could rival for any other disease. In terms of innovation, this drug was truly innovative. Velcade is a traditional drug that is now revolutionizing the treatment of multiple myeloma. But, it is not a protein based biologic and therefore gets 3 years of exclusivity. There are many other similar examples that demonstrate that the level of innovation and benefit to society is every

bit as great with traditional drugs compared to biologics. The argument that biologics are more innovative or more valuable to society and therefore deserve longer periods of exclusivity is simply not supported by the array of currently marketed products.

Finally, it is important to note that the law currently includes several, significant incentives for brand biologic makers. For example, biologic drugs can take advantage of the 7-year orphan drug exclusivity period. Biologic patents also can be eligible for the patent term extension provisions enacted as part of Hatch-Waxman.

1 – DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: Is biotech different. Managerial & Decision Economics. 2007 28 :469-479

8. What are the appropriate factors to consider when determining the optimal length of regulatory exclusivity periods for biologic drug products? Do these factors change based on the type of referenced product involved, the extent of competition facing the referenced product, or patent portfolios claiming the referenced product, and if so, how?

Response: In 1984, Congress carefully considered the length of regulatory exclusivity that brand companies should receive for developing innovative products. The Drug Price Competition and Patent Term Restoration Act (also known at Hatch-Waxman) struck an effective balance between competition and innovator protection. The length of exclusivity afforded by Hatch-Waxman does not vary according to the referenced product, the extent of competition, or patent portfolios claiming the referenced products. One standard has suited the entire marketplace, where innovator companies have continued to produce new therapies and increased competition among drugs has lowered the cost of pharmaceuticals.

If Congress believes that brand biologic makers need an additional incentive, the exclusivity provisions outlined in Hatch-Waxman should appropriately extend to biologics. The five-year exclusivity for new, innovative traditional drugs has been more than sufficient to foster significant pharmaceutical innovation, as hundreds of traditional drugs have been approved since 1984. Based on this history of solid innovation in the traditional drug space with five-year exclusivity, there is little, if any, evidence that a longer period would be justified.

9. How does the European Medicines Agency's approach to regulatory exclusivities in its abbreviated regulatory approval pathway for follow-on biologics inform the U.S. approach?

Response: When generic biologics were introduced in Europe, the European Medicines Agency (EMEA) applied the same regulatory exclusivity provisions to both small molecule pharmaceuticals and biologics. In our view, the US similarly should adopt the same regulatory exclusivity provisions for both small molecule pharmaceuticals and biologics. There should be one consistent standard for all products.

10. Is a marketing exclusivity period necessary to encourage companies to develop follow-on biologics and to seek their approval by the FDA? If so, why, and how should such an exclusivity period be structured?

Response: CCPM supports innovation by both brand and generic companies. Innovation is encouraged by a balanced legislative process that spurs brand and generic industries to expand consumer access to new branded drugs and affordable generic versions of previously approved biologics.

Patent Dispute Resolution Issues

1. Would it be important to have the litigation of any patent disputes proceed concurrently with the abbreviated FDA approval process for follow-on biologics? Why or why not? What has been learned from the experience under Hatch-Waxman about the incentives necessary to encourage early resolution of patent issues?

Response: For consumers to realize meaningful savings from generic biologics, legislation establishing the approval pathway must include an efficient patent dispute resolution process. The BIO-sponsored proposals introduced to date do not contain such a process. Allowing the brand company or a third party to time the assertion of patents to the filing of generic applications, or to otherwise manipulate the legal process, will only lead to delayed market entry and thus delayed savings to consumers. Congress should enact a voluntary system under which certain patents can be asserted prior to the generic company's market entry. H.R. 1038, the Access to Life-Saving Medicine Act, contains such a process. The process outlined in H.R. 1038 takes advantage of the tough lessons learned with Hatch-Waxman; in particular how some brand companies have used weak or suspect patents to obtain automatic 30-month stays of generic drug approvals.

2. How long might the approval process for a follow-on biologic application take? What factors might influence this timing?

Response: The timing of the approval of generic biologics, like the timing of traditional Hatch-Waxman generics, will depend in large part on the resources that FDA can allocate to reviewing such applications. We therefore urge Congress to provide FDA with the resources necessary to promptly review and act upon all generic applications, including generic biologics applications. We also note that some pending generic biologics bills include user fees for generic biologics. Assuming companies submitting applications for generic biologics pay user fees, applicants should expect and receive particularly timely reviews and approvals.

3. How might differences between patent portfolios for small molecule drugs and biologics affect patent litigation involving follow-on biologics? How long might patent litigation involving a follow-on biologic product take?

Response: We are not aware of differences between the patent portfolios for small molecule drugs and biologics that might affect patent litigation involving generic biologics. How long brand/generic biologic patent litigation will take most likely will be dictated by the patent dispute resolution mechanism that Congress ultimately enacts. If Congress enacts a system like that found in H.R. 1038, we believe that patent disputes could be timely resolved such that the launch of generic biologics would not be unduly delayed. If, however, Congress enacts a system backed by BIO, litigation (even over weak or suspect patents) would significantly delay generic market entry, which would hurt consumers and third-party payers.

4. When is it in the interest of a referenced biologic drug manufacturer to resolve patent issues prior to marketing by a follow-on applicant? When is it in the interest of a follow-on biologic applicant to resolve patent issues prior to marketing its follow-on biologic? When is it in the interest of either party to resolve patent issues following commercial marketing of the follow-on product?

Response: It is in a generic company's best interest to litigate prior to actually marketing its product only those patent disputes that would delay its launch. Significantly, the need to resolve patent disputes pre-launch will not exist with respect to every brand patent. The voluntary system outlined in H.R. 1038 recognizes this fact and allows the generic company to identify the patents that it wishes to litigate pre-launch, and allows the brand company to litigate its remaining patents after generic launch.

If it can bring suit on all of its patents immediately, it is in the brand company's best interest to do so precisely because it will delay generic market entry. As previously discussed, some BIO-supported bills allow the brand company or a third party to time the assertion of patents to the filing of generic applications or otherwise manipulate the legal process, which will only lead to delayed market entry and thus delayed savings to consumers.

5. What are the legal impediments facing a follow-on biologic applicant that has not been sued for infringement to obtaining a declaratory judgment on patent infringement or invalidity issues prior to commercial marketing of its follow-on product?

Response: In light of the U.S. Supreme Court's decision in *MedImmune*, as well as the subsequent Federal Circuit decisions recognizing the impact of that decision on the so-called "reasonable apprehension" test for declaratory judgment (DJ) jurisdiction, we do not anticipate any legal impediments to DJ actions in the FOB context. We nevertheless encourage Congress to enact DJ provisions for generic biologics along the lines of those included in the 2003 the Medicare Prescription Drug, Improvement, and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003) (codified at 21 U.S.C. § 355(j) and 35 U.S.C. § 271).

6. Are regulatory exclusivities needed to encourage follow-on biologic applicants to challenge patents? Why or why not?

Response: CCPM supports innovation by both brand and generic companies. Innovation is encouraged by a balanced legislative process that spurs brand and generic industries to expand consumer access to new branded drugs and affordable generic versions of previously approved biologics.

7. What opportunities will biologic drug manufacturers and follow-on applicants have to manipulate proposed new regulatory obligations (e.g., application notification obligations, declarations of patents claiming biologic drugs, etc.) and exclusivity periods surrounding a concurrent patent resolution process? What are the prospects for the improper use of citizen petitions to delay approval of follow-on biologic applications?

Response: CCPM has significant concerns about various provisions in several of the BIO-sponsored bills in terms of their potential for abuse that would delay generic market entry. For example, bills that include provisions erecting unnecessary barriers to generic approvals (provisions such as mandatory guidance or rulemaking processes) could be manipulated by brand companies in order to significantly delay generic market entry. The same is true of BIO-sponsored bills that would allow exclusivity received based upon approval of a single new indication to block generic approval for all indications. With respect to citizen petitions in particular, we note that H.R. 1038 contains provisions specifically designed to prevent any abuse of the petitioning process. Alternatively, Congress could expand the citizen petition provisions of the 2007 FDAAA to generic biologics. Either way, we encourage Congress to include provisions designed to prevent citizen petitions from unnecessarily delaying generic market entry.

8. How might referenced biologic product manufacturers and follow-on biologic applicants structure patent settlement agreements given the competitive dynamics arising from the marketing of follow-on biologic drugs? What incentives might exist for these companies to enter anticompetitive settlements? Should patent settlement agreements be filed with the antitrust agencies? What would be the likely effect of the filing requirement on settlements?

Response: As the FTC is aware, the Medicare Modernization Act of 2003 ("MMA") includes a provision requiring that agreements between brand and generic companies be reported to both the FTC and DOJ, which allows these agencies to review the terms of such agreements. Expanding the MMA reporting requirements to cover generic biologics would be a logical step for Congress to take.