PCMA
PHARMACEUTICAL CARE MANAGEMENT ASSOCIATION

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

RE: ''Emerging Health Care Competition and Consumer Issues—Comment, Project No. P083901''

Dear Commissioners:

The Pharmaceutical Care Management Association (PCMA) is grateful for the opportunity to submit comments in conjunction with the Federal Trade Commission's (FTC) workshops on emerging health care competition and consumer issues. Developing an abbreviated regulatory approval pathway for generic biologic drugs is critical to ensuring robust competition in the biologic drug marketplace and expanding consumers' access to affordable, life saving drug treatments and therapies.

PCMA is the national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans for more than 210 million Americans with health coverage provided through Fortune 500 employers, health insurance plans, labor unions, and Medicare Part D.

Attached, please find PCMA's prepared responses to the questions posed by the FTC in the September 3, 2008 Federal Register notice of the upcoming public workshop.

Sincerely,

Missy Jenkins
Senior Vice President, Federal Affairs

Regulatory Exclusivities and Follow-on Biologic Drug Competition

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?**

   PCMA is very confident that the introduction of generic biologics will increase competition and reduce overall drug spend, specifically for generic biologics that are deemed interchangeable. The impact on cost will depend on the number of generic biologics introduced, the ability to interchange the drugs, and the number of branded products that are already on the market. For example, several growth hormone products are currently available in the market. As such, physicians are accustomed to selecting from a variety of products when prescribing and are likely comfortable with the interchangeability among branded growth hormone products.

   The level of success for generic biologics will also likely be linked to the disease state(s) for which they are used. For example, a drug like erythropoietin where the outcome variable is an easily measurable surrogate endpoint (i.e. an increase in hemoglobin) will likely have more success than a drug such as Rituxan, where the outcome of therapy would be remission versus progression of cancer. Prescribers may be more willing to use a generic biologics where the outcome of therapy can be easily and quickly measured, i.e. hemoglobin levels or white blood cell counts, versus one where the outcome could be death or progression of the disease.

   In terms of how competition has developed between referenced and generic biologics in European markets, erythropoietin (EPO) can serve as an example. It is important, however, to consider the different market structure utilized by the European Union as price controls are not a market variable in 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 EU, 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. IMS data shows that 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 generic EPOs appear to be priced approximately 25 - 30 percent below where the innovator price was prior to the entry of any generic competitor.

   In the U.S., reference product manufacturers would likely endeavor to combine lower prices with increased marketing activities in response to generic biologics. The growth hormone market could show this trend, as Novartis has introduced Omnitrope pen devices at almost a 50 percent discount off other branded devices. While a large shift to Omnitrope will happen over time, eventually brand name manufacturers will be driven to provide price concessions to address this level of price differential between major brands and new competitors in this marketplace. The overall benefits of which will be in the form of lower costs to payers and consumers.

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?**

   In the absence of an interchangeable designation, it will take much longer for the generic biologic 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. The movement to the generic biologic may eventually take place after a large amount of experience has been gained in the market.

   If the generic biologic is designated interchangeable, the effect will be a more rapid infiltration into the brand market share. Since 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. In the managed care, mail-service environment, non-biologic drugs deemed to be interchangeable achieve upwards of a 90-95% substitution rate in as little as one month following introduction. While the rate of uptake is slower in the retail environment, for many products this same rate is achieved in six months to one year. This creates enormous cost savings for the payor which are passed on to 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.

   There would likely be differences in conversion from brand to the generic biologic in either scenario outlined above based on the indications for use of the drug. Drugs used to treat very serious conditions (e.g., cancer), where failure of the generic biologic could have irreversible consequences may face a more formidable marketplace challenge, likely based on perception and not science. However, drugs used to treat less serious conditions (e.g., growth hormone and EPO) likely face reduced obstacles.

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?**

   The Medicare Modernization Act of 2003 (MMA) requires that all patent litigation settlements in which the brand manufacturer financially compensates the potential generic competitor to delay entering the market be filed with the FTC and the DOJ. 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?**

   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. A science-

based pathway creates a streamlined process empowering the FDA to employ its high safety standards to independently determine approval for these products. 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 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.

Hatch-Waxman created a science-based generic approval pathway that effectively balances the need for competition and reduced drug prices with the need for continued innovation. The result has been a positive effect on research and clinical programs throughout the U.S. while improving access to less costly medications. There is no reason to believe a generic biologics approval pathway would have any less positive effects in the biologics arena if adopted in the mold of Hatch-Waxman. However, a pathway with burdensome obstacles to generic approval or unduly long market exclusivity periods for branded biologics would lead to less innovation and less incentive to compete in the biologics arena. In testifying before Congress, the FDA had acknowledged the ethical considerations with respect to requiring redundant clinical trials with known results.

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?**

Medicare's current method for reimbursement will likely result in reduced pricing for referenced biologic products.

Biologics administered in the physician's office are reimbursed through codes defined by CMS's Healthcare Common Procedure Coding System (HCPCS) and the American Medical Association's Current Procedural Terminology (CPT). Whereas National Drug Codes (NDC) for the same products vary by manufacturer, strength and dosage form, the HCPCS/CPT system groups multiple similar products together with one code.

This difference can be illustrated by Epogen and Procrit, which treat anemia associated with renal disease and cancer treatments. There are more than 35 NDCs for those products, representing the various doses. Only two HCPCS codes are used for these products: J0886, epotein alfa for end stage renal disease (ESRD) and J0885, epoetin alfa for non ESRD. Physician reimbursement is based on the average sales price (ASP) for all Epogen and Procrit. Not surprisingly, Epogen and Procrit are priced very similarly.

ASPs are reported quarterly and reimbursement is based on a two quarter lag on this data. Thus, when a generic biologic enters this class at a reduced price, it will share the same two billing codes as Epogen and Procrit. Doctors who immediately utilize the generic product will improve their bottom line by saving the difference between cost and reimbursement. After the six month delay, the ASP will fully reflect the impact of the lower cost product. This may create a reimbursement challenge for physicians who continue to use the reference product, as the ASP may not cover the drug's acquisition cost. To this end, Medicare's reimbursement model will quickly spur adoption of generic biologic use.

The most important factor to spur physician adoption will be to update the Medicare reimbursement system so bioequivalent products are reimbursed with the same codes. Because of shared reimbursement codes, doctors would be incentivized to utilize generic biologics. Additionally, it is important that generic biologics shares 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.

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

Brand biologic drug products are protected by patent portfolios (often extensive portfolios), as are 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 benefit from 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. Innovators will very likely defend their patent rights against generic biologics just as ardently as 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?**

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).[1] Therefore, there appears to be little financial argument for a greater period of exclusivity for biopharmaceutical products based on R&D costs.

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 as such 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 better treatment alternatives for patients with this condition. These small molecules receive the standard 3-year exclusivity, even though they are superior to the large molecule protein for this condition.

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

Gleevec, another small molecule drug that receives 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 a leader. Velcade is a traditional drug that is now revolutionizing the treatment of multiple myeloma. But, it is not a protein based biologic and therefore receives 3 years of exclusivity. There are many other similar examples that demonstrate 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.

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?**

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.

The exclusivity provisions outlined in Hatch-Waxman should appropriately extend to biologics. The 5-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. Additionally, this would be consistent with the model of the EU, where generic biologics are not afforded exclusivity any differently than non-biologic generic drugs. Based on this history of solid innovation in the traditional drug space with 5 year exclusivity, there is little 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?**

When generic biologics were introduced in Europe, the European Medicines Agency (EMEA) applied the same regulatory exclusivity provisions to both small molecules pharmaceuticals and biologics. In our view, the U.S. should similarly 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?**

PCMA 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.