May 2, 2008

The Honorable Frank Pallone, Jr.
Chairman
House Energy and Commerce Subcommittee on Health
United States House of Representatives
316 Ford Office Building
Washington D.C. 20515

The Honorable Nathan Deal
Ranking Member
House Energy and Commerce Subcommittee on Health
United States House of Representatives
316 Ford Office Building
Washington D.C. 20515

Dear Chairman Pallone and Ranking Member Deal:

Thank you for your joint letter of April 3, 2008, in which you posed several questions related to the creation of a legislative pathway for the Food and Drug Administration (FDA) to approve generic biologics.

In drafting the attached responses, I have relied on the expertise of the member organizations of the Coalition for a Competitive Pharmaceutical Market (CCPM). If you or your staff have any questions regarding our answers or require additional information, please don't hesitate to let me know.

On behalf of CCPM, thank you for your continued interest and attention to this important subject. We look forward to working with you and members of the committee to get meaningful legislation passed this year.

Sincerely,

Annette Guarisco

Annette Guarisco
Chairman

cc: Honorable John D. Dingell, Chairman, House Committee on Energy and Commerce
Honorable Joe Barton, Ranking Member, House Committee on Energy and Commerce
Melissa Sideman (via email)

Coalition for a Competitive Pharmaceutical Market
May 2, 2008

Science/Safety

1. What is immunogenicity? Why is immunogenicity a special concern for biologics and what are the risks to patients? Do immunogenicity risks vary depending on the type of biologic?

   Response – Immunogenicity is the potential for a drug to cause an immune response in patients. Most immunogenic responses are weak and result in little to no effect on patients. A small proportion of immunogenic responses can result in an allergic response or neutralizing effect on the biologic. Immunogenicity risks may vary depending on the type of biologics. Some biologics have little or no immunogenic response based on clinical data.

2. To what degree, if any, is immunogenicity testing necessary? Should immunogenicity testing be mandated by statute for all follow-on biologics (FOBs) or should the Food and Drug Administration (FDA) be given discretion to determine whether such studies, and what types of studies, are needed on a case-by-case basis?

   Response – FDA should determine whether immunogenicity testing is necessary on a case-by-case basis. The FDA is in the best position to make that determination based on sound science and should have adequate resources.

3. Has FDA exercised appropriately its discretion whether to require immunogenicity testing for manufacturing changes? Should immunogenicity testing for manufacturing changes be mandated by statute, or should FDA be given discretion to determine whether such testing is necessary?

   Response – Yes, FDA has exercised appropriate discretion as to whether to require immunogenicity testing for manufacturing changes. A case-by-case approach is the most effective course. The FDA is in the best position to make that determination based on sound science and its considerable experience with these products.

4. Should FOB applicants have to provide evidence of similarity, safety, and effectiveness of each indication separately or can evidence for one indication be extrapolated to another?

   Response – A FOB applicant that provides the evidence required by the FDA for one indication should be granted approval for all indications

sharing the same mechanism(s) of action, to the extent that the mechanism(s) of action is known.

5. Under the Food and Drug Administration Amendments Act of 2007, Congress established new authorities for FDA to enforce drug safety. How should the new post-market authorities enacted in this legislation be applied to FOBs? Are post-market studies always needed for FOBs? Are there situations in which FOB applicants will need to conduct post-market studies that are different from those that have been required and/or requested for the reference product?

   Response – FDA should be allowed to use the safety history of the innovator product to determine what, if any, post-market studies should be required by the FOB applicant. The requirement, however, should not go beyond what was or is required of the innovator product.

6. Should non-interchangeable FOBs be required by statute to have different non-proprietary names from the reference product? What should the standard be for interchangeable FOBs? What are the advantages and disadvantages of requiring different non-proprietary names, including any affect on patient safety? What alternatives are available?

   Response – There should be no statutory requirement for separate and distinct names for FOB when FDA determines that the scientific data demonstrates that the FOB has similar composition compared to the reference product. The FDA has rejected brand industry requests for unique non-proprietary names. In a September 1, 2006 statement, FDA stated that the agency did not believe that a unique non-proprietary name should be assigned. Different names will create confusion among doctors and other health care practitioners and patients, and hinder full competition. FDA should use uniform nomenclature when describing FOBs so consumers, physicians, pharmacists, and others can make informed, value-driven decisions about pharmaceuticals and treatments. It is critical to use consistent terminology in order to maximize competition among brand biopharmaceuticals and biogenerics.

7. Is it important that an innovator and an FOB have the same mechanism of action? Why or why not? If the mechanism of action of the reference product is unknown, should the FOB applicant be required to determine the mechanism of action and ensure that both products share the same one? Why or why not?

   Response – The mechanism of action for drugs may be unknown, but, nevertheless, FDA has found those drugs to be safe and effective in light of the data submitted. Where the mechanism of action is unknown, the FOB applicant should not be required to determine the mechanism of action. The similarity of the FOB to the reference product can be firmly established through biochemical analysis.

8. How much variability in chemical structure is there in individual brand biologics: (1) batch-to-batch, and (2) as a result of manufacturing changes? What are the implications, if any, for FOBs testing requirements, naming, and interchangeability?

   Response – There is very little or no variability to the amino acid sequence, which is the majority of the biologics's protein chemical structure. Certain expected variability that meets specifications is allowed, but it does not impact clinical performance and is standard for synthetic compounds. The analytical testing of variability will be the same for the innovator as it is for the FOB batch-to-batch or during manufacturing changes.

9. Should human clinical trials be mandated by statute for all FOBs or should FDA be given discretion whether such trials are needed on a case-by-case basis? Would not requiring human clinical studies of FOBs result in these products having a more difficult time reaching market acceptance? Why or why not?

   Response –As is done today, the FDA should be given discretion on a case-by-case basis to determine what, if any, clinical trials are needed. As a general ethical principle, patients/volunteers should not be subjected to unnecessary clinical trials. If comparability can be clearly established for well characterized molecules with a known mechanism of action through analytical, non-clinical assessments, the agency can approve the product without the clinical efficacy comparability assessment.

10. What studies have been required for past approvals of protein products under section 505 of the Federal Food, Drug, and Cosmetic Act (FFDCA)? Have any been approved without clinical trials?

    Response – To date, there is variability in the range of studies the FDA has required for protein products submitted under section 505 of the FFDCA. It is our understanding that the agency has indicated for some protein products, extensive comparative characterization along with PK/PD studies are sufficient.

11. Omnitrope is approved in the U.S. (albeit as a 505(b)(2) and in Europe (as the first biosimilar).

    - Have patients experienced any problems?

    - Have patients been switched to Omnitrope from other recombinant human growth hormone products?

- If the answer to part b is yes, how are payers handling the availability of this comparable product?

Response – Right now there are more than 7 somatotropin (human growth hormone) products on the market. All of these products have distinct proprietary names, but the same generic name. Some of these products have been on the market for more than a decade. We have not identified, at this time, any unusual problems with Omnitrope. Furthermore, it has been common practice for years to treat all somatropin products as interchangeable from a formulary perspective.

Patients likely have been transitioned from other somatropin products to Onmitrope, just as this has happened with other somatropin products for years.

For the purposes of formulary placement, almost all payers treat somatropin products as interchangeable. The similarity of dosage forms, e.g. prefilled syringes, seem to be a more relevant concern in terms of interchangeability than the proprietary name of the product selected. Formulary products are covered at a lower copay than non-preferred products, and sometimes the non-preferred growth hormone products are not covered at all.

Regulatory/Administrative

1. Some believe Section 505 of the FFDCA provides a regulatory pathway for approval of biosimilars for reference products approved under Section 505. Should a newly created biosimilar regulatory approval process include all biologics approved under the FFDCA as well as those regulated under the Public Health Service Act?

   Response -- S. 1695, "The Biologics Price Competition and Innovation Act of 2007," moves 505 biologics to the PHSA, but creates an exception. Under that exception, a 505(b)(2) or ANDA can be filed under the FFDCA if it is submitted within 10 years of enactment of the bill. We believe the approach taken in S. 1695 is appropriate. To the extent that biologics approved under the FFDCA eventually get moved to the PHSA, those products should not benefit from any exclusivity or other incentives that Congress might create for drugs approved under the PHSA. To do so would be to severely harm consumers and taxpayers.

2. The current statute gives FDA discretion to decide whether a change in an approved biologic requires assessment through a clinical trial. Do you think this statutory discretion has been appropriate or adequate? What has been its effect on patient safety?

Response – This statutory discretion has been appropriately used by FDA and we have not seen any effect on patient safety.

3. What FDA office should review FOBs?

   Response – We support the position taken in S.1695 which requires the same group within FDA that reviewed the brand application to review the FOB application. In order to adequately and appropriately review and assess these products additional resources are necessary.

4. What standards are required to assure sufficient similarity between the FOB and the reference product? Is the requirement that the FOB be "highly similar" to the reference adequate or should an applicant be required to establish that the FOB is "as similar as scientifically as possible"? How would FDA assess these requirements?

   Response – The FDA should develop standards in a timely manner and on a case-by-case basis based on their experience with and knowledge of the reference product and the FOB submission. The FDA describes its approach for evaluating FOBs and related products in a white paper entitled The FDA's assessment of follow-on proteins products: a historical perspective (April 2007):

   > In all cases, when assessing applications for protein products that were similar to prior products, the FDA has considered a number of factors, including the robustness of the manufacturing process, the degree to which structural similarity could be assessed, the extent to which mechanism of action was understood, the existence of valid, mechanistically related pharmacodynamic assays, comparative pharmakinetics, comparative immunogenicity, the amount of clinical data available, and the extent of experience with the original product, or products.

5. Should FDA be required to promulgate regulations and guidance before reviewing applications? Why or why not? Furthermore, should FDA be required to issue and permit public comment on product-specific guidance before submission of applications? What are the advantages and disadvantages? How long will it take to put a regulatory framework in place, including new regulations and guidances for FOBs?

   Response – Science should guide the process, and the FDA should be allowed to review and approve FOB applications before guidances or regulations are issued. After the passage of Hatch-Waxman in 1984 the agency reviewed and approved thousands of ANDAs before the final regulations were published in 1992 and 1994. As is the practice with the review and approval of a novel product, the FDA and the sponsor of the

NDA develop the plan, science drives the process, and there is no guidance or public comment. In addition, the review of ANDAs could also assist in the development and implementation of appropriate guidances.

We oppose a mandatory guidance process for FOBs, because it is unprecedented, unnecessary, unproductive, and will be used as a delay tactic for the actual approval of safe and more affordable products.

6. How much in additional appropriations or user fees would FDA need to implement a generic biologics program? What proportion of resources should come from user fees? How would that relate to the user fees that are assessed for traditional drugs and/or biologics?

   Response – CCPM supports user fees as one way to fund the manpower necessary to approve FOBs. The fee should be established based on resources need of the Agency and include performance metrics for these applications.

Interchangeability

1. Does current science permit an assessment of interchangeability (substitutability) for any biologics at this time? What is the likelihood that interchangeability assessments for some or all biologics will be possible in the future, and in what period?

   Response – Yes, based on the scientific data generated on Hospira's product Retacrit™, FOBs can be interchanged with the innovator. Interchangeability assessments can and are being done now.

   We strongly believe that the science should drive the process and the scientific experts at the FDA should have the flexibility to make determinations of interchangeability. This is the best way to encourage the development of strong, cutting edge technology and science.

2. In general terms, what types of testing or data would be necessary to establish that two biologics are interchangeable?

   Response – The FDA should be given the authority to determine what studies are necessary for each individual FOB applicant. Some of those studies might include analytical studies such as the assessment of immunogenicity and/or pharmacokinetics or pharmadynamics.

3. How should product-specific requirements for demonstrating interchangeability be established? Should the statute prohibit interchangeability assessments or give FDA the authority to determine interchangeability as science permits? Please explain your answer.

   Response – As stated above, the FDA should be given the authority to determine interchangeability on a case-by-case basis based on the scientific evidence. Requirements, such as product-specific guidances, will only serve to delay competition.

4. Should there be product specific guidances, with opportunity for public comment, on establishing interchangeability before submission of applications? What are the advantages and disadvantages?

   Response – Product specific guidances should not be required of the FDA before the agency can accept and approve an FOB application. As we stated earlier, the existence or nonexistence of a guidance should not restrict the agency from reviewing or approving an FOB application. Not allowing products to go forward in the absence of guidance would greatly diminish the ability of the public from benefiting from these products thus delaying market entry for years. Guidances should not delay scientific review or approval of FOB applications.

5. What are the potential risks to patients from interchangeability of one biologic for another? If FDA finds two biologics interchangeable, should physicians, pharmacists, and patients feel comfortable with substitution by pharmacists? Why or why not? How would interchangeability affect patient access to biologics?

   Response -- If using all of its knowledge and expertise, the FDA finds that two protein-based drugs or biologics are similar and, therefore, interchangeable with each other, then patients and heath care providers should feel secure in substituting one for another.

6. How would interchangeability affect competition in the market place, and/or reimbursement by health plans? Will it affect the costs of biopharmaceuticals?

   Response – The determination of interchangeability among originator and follow-on products will have a positive impact on competition in the marketplace. It will provide health plans and payers with greater flexibility in formulary decision making and coverage. The cost for the biopharmaceuticals and FOBs will be made more affordable because of the competition for formulary placement and plan coverage.

   In terms of reimbursement by plans, both the follow-on and originator product will likely both be covered, but the lower cost product will be

covered at a lower copayment for members. Given that some of these therapies cost well in excess of $10,000 per year, and sometimes as much as $100,000 per year per patient, price competition is vitally important in the biologics arena. Even a 20% discount on cost is a significant win for a drug that costs $20,000 a year. So, even if FOBs do not have the type of pricing discounts that are available for traditional generic products today, there is still a significant savings to be realized from interchangeability with these drugs.

Patents

1. In your view, how long is the current effective patent term for pharmaceuticals? Specifically, how long on average are drugs marketed under patent protection following FDA approval?

   Response – Typically, all brand-name drug products, whether a small molecule or biological, are protected by a broad range of patents. Typically, the patent holder obtains these patents over time, rather than all at once, for the purpose of stretching out its patent protection for as long as possible. From our review of the FDA Orange Book, which relates to traditional small molecule drugs, it appears that brand companies routinely obtain patents that extend years beyond FDA approval. The same is true for biologics. For example, FDA approved Amgen's EPO product in 1989 and Amgen has stated that it has patents still protecting this product, nearly 20 years after FDA approval.

2. The Hatch/Waxman Act restored innovator patents up to 14 years, and further provided manufacturers with 5 years of data exclusivity. Is this a good model for biologic manufacturers? What lessons can we learn from the Hatch-Waxman Act, and apply towards Congress's discussion about FOBs?

   Response – As we understand it, biologics makers have been able to enjoy the Hatch-Waxman patent term restoration provisions since Congress enacted them in 1984. When it comes to regulatory exclusivity, biologic makers should not receive any more exclusivity (in terms of years or the types of products eligible for exclusivity) than that provided for in Hatch-Waxman. Hatch-Waxman strikes the right balance between innovation and generic access. Providing more exclusivity for biologic manufacturers would tip the balance against consumers and taxpayers, which will result in the loss of billions of dollars a year in badly needed savings.

3. Please explain if patents on biotech medicines will provide meaningful protection of intellectual property if a pathway is created to allow for the regulatory approval of FOBs? How do patents on biotechnological medicines compare or differ in the value they offer to traditional small-molecule drugs, if an FOB's pathway requires only that the FOB be highly similar to the reference product?

Response – To our knowledge, no one has provided an objective analysis establishing that biological drug product patents have less value than the patents protecting traditional drugs. Indeed, 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. We believe that innovators will as ardently defend their patent rights against FOBs as they do today against chemical generic applicants.

4. What procedures, if any, should be included in legislation to enable reference product companies or third parties to identify potential patent infringement claims by a biosimilar company and to ensure timely resolution of legal disputes?

   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 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.

5. If patent issues are to be addressed in a statute, how should we balance the interests of third-party patent holders and the reference product sponsor?

   Response – As noted above, generic biologics legislation must include an efficient patent dispute resolution process. Legislation that allows a large number of patents, whether owned by the brand company or a third-party, to be asserted against the generic after the submission of its application would significantly and unfairly delay generic market entry. Again, Congress should enact a voluntary system, such as the one in H.R. 1038, under which certain patents can be asserted prior to the generic company's market entry. If a third-party owns one of those patents, the legislation should contain a mechanism for involving that third-party in the voluntary system.

6. Should an FOB statute require FDA to administer patent listing and notification provisions as Hatch-Waxman does? Has this process been an appropriate and efficient use of FDA's resources and expertise? Why or why not? Can appropriate notification be accomplished through an alternative process that does not enlist FDA resources?

Response – FDA should focus its efforts where its expertise lies—reviewing and approving drug applications based on sound science. We believe that Congress can create an efficient patent dispute resolution mechanism for generic biologics products that does not involve FDA.

Incentives/Exclusivity/Investment

1. Should reference product manufacturers be given a period of exclusive marketing in addition to the patent-term restoration already provided to them under Hatch-Waxman? If yes, how much is necessary to provide adequate incentives for innovation without unnecessarily delaying competition?

   Response --To the extent Congress decides to give biologic products marketing exclusivity, it should be the same as traditional drugs, i.e., 5-years for a limited category of products. The 5-year exclusivity for traditional drugs has clearly been sufficient to foster significant pharmaceutical innovation over the past 20 years, as hundreds of new and innovative traditional drugs have come to the market.

   Clearly, drug therapy advances coming out of the traditional drug pipeline over the past 20 years have been as great as, if not greater than, biologics. Consequently, it is difficult to understand why an exclusivity period longer than currently exists under Hatch-Waxman would be considered.

2. What types of assessments have been conducted to determine the minimum term of exclusivity that will enable a robust industry for discovery and development of biologics?

   Response – We fundamentally disagree that investment in biologics will diminish without exclusivity. The U.S. pharmaceutical industry already accounts for investment when they price their products. We are not aware of any objective studies other than brand-supported statements, supporting the need for additional incentives for branded biologics to stimulate investment. Patent protection, patent restoration, and other laws such as the Orphan Drug Act offer abundant incentives. Adding market exclusivity to current patent incentives presupposes that they are necessary for investment.

3. How should exclusivity for modifications to approved products be addressed?

   Response – As noted above, we believe that Hatch-Waxman provides a good model for any exclusivity that Congress is considering awarding to biologics. It should be noted, however, that biologic makers currently enjoy a number of incentives. For example, they can take advantage of Hatch-Waxman's patent term restoration provisions and the 7-year Orphan Drug Exclusivity provisions.

4. What benefits do innovator firms obtain from data exclusivity, and how is this protection different from patent protection?

   Response - Data exclusivity prohibits a generic manufacturer from filing an application with the FDA. There can be no opportunity for competition during this period as the exclusivity is absolute and not subject to challenge. A patent, on the other hand, can be challenged. Consequently, it is entirely possible for an innovator to have invalid patents but still reap the benefits of market protection against competition. This could have the affect of discouraging innovators to pursue legitimate patents. In addition to being absolute, exclusivity also fails to take into account investment or innovation. That is, company A investment $3 billion to develop Biologic 1 and works for all patients, while Company B invests $1 million to develop Biologic 2 which works for less than half of all patients, yet both get the same amount of exclusivity. The market, not preordained monopolies, already account for this disparity through pricing.

   Valid and enforceable patents on an innovator's product provide a means of protecting the innovator's product against an infringing generic product. The benefit of the exclusivity period is that no generic manufacturer can even have the opportunity to produce a competing product during this period, and there would be no opportunity to engage in patent litigation during this period because the generic applicant would not have standing since there would be no application.

5. Do you think biologics should receive a different period of data exclusivity than drugs? Why or why not?

   Response – There is no objective data justifying why biologic products would need exclusivity beyond what was established under Hatch-Waxman. The five year exclusivity for 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 evidence that a longer period would be justified.

6. What policy considerations justify that patent protections be the principal form of intellectual property protection for biologics and drugs?

   Response - Patent protection is the incentive for innovation. The rationale behind patent protection is that the inventor is rewarded because there is some public benefit associated with their invention. The same is true with patents protecting drugs. The monopoly that comes with market exclusivity does not provide a similar incentive for innovation. Having

patents as the principle form of protection will act as an incentive to new innovation. As discussed above, there are other incentives for innovation under the existing law such as Orphan Drug Exclusivity.

7. If a follow-on biologics pathway was created without additional incentives—beyond existing patent protections—for continued innovation, how would innovation be affected either positively or negatively? What additional incentives, if any, would be necessary to support continued research and innovation, including at American universities?

   Response – We do not believe that additional incentives are necessary to encourage innovation. Even if there were no exclusivity (which there already is for many biologics products under the Orphan Drug provisions), prices for biologics would still reflect investment and projected profits, as they do now. This past year, brand drug costs rose by an average of nearly 8% to meet financial and shareholder expectations. That investment would remain even if no additional exclusivity was granted.

Economic Impact

1. How much savings would a generic biologics pathway create and in what period (taking into account the time it will take to implement any new law, and the time needed by manufacturers to develop products and submit applications)? Please describe the evidence on which you base your answer.

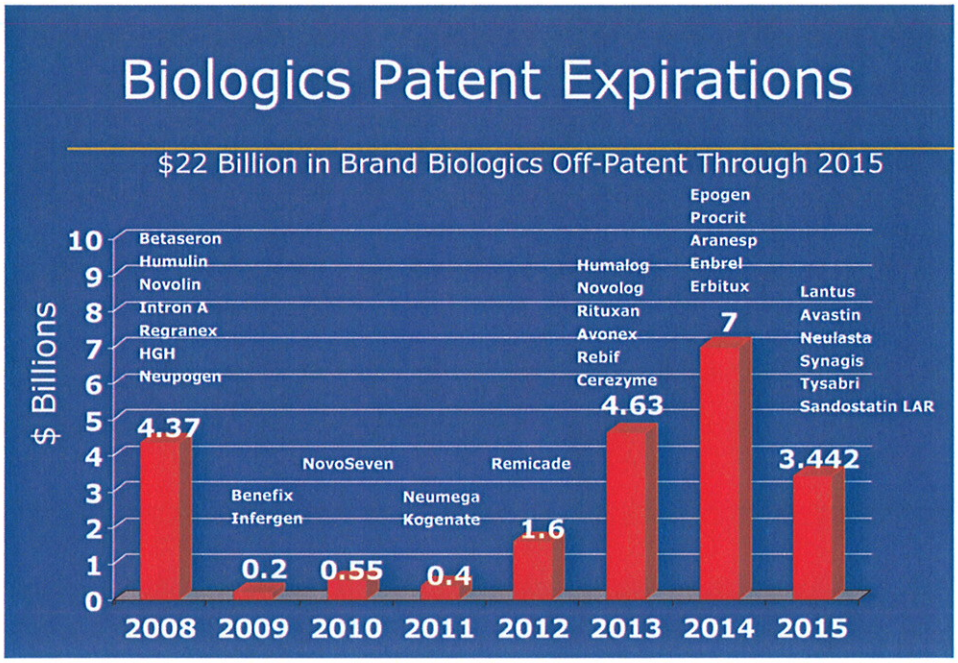
   Response -- Multiple savings estimates have been released over the last eighteen months. Express Scripts analysis considered four therapeutic areas across the entire market and concluded there was a ten year $71 billion dollar savings opportunity. Avalere Health released a ten year forecast on savings 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. Can you provide an estimate of the amount of money your agency/company will spend on biological products over the next 10 years, in absolute dollars, and as a percentage of total program/plan spending? If FOBs, approved by FDA as comparable to the brand name product, were available, what is your estimate for the cost of the reference product and the follow-on product?

   Response – If the follow-on is interchangeable with the originator's brand, the discounts on the follow on could be 30 to 40 % off the brand price. This will, of course, depend on how many follow-ons enter the market. The more follow-on products that enter the market, the higher will be the discounts off the reference product price.

3. What implications would a follow-on biologics pathway have on U.S. economic competitiveness and leadership in protection of intellectual property rights?

   Response – A science-based, follow-on 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 world-wide through heightened capital investments. The pathway will not affect valid and enforceable patent rights in any way.

4. What implications does the treatment of patents in the context of a follow-on biologics approval pathway have for the future of biotechnological innovation?

   Response – U.S. competition law is based on the premise that competition breeds innovation, and monopolies stifle innovation. Patent-holders for biologic medicines exercise monopoly power for a specified period of years based on patent protection, but under a new pathway will also exercise market exclusivity. Those patent holders, like other monopolists, have little incentive to innovate. Any biologics pathway that is strewn with administrative pot holes and other delay devices such as unclear patent resolution mechanisms would similarly perpetuate brand company monopolies and create substantial disincentives for innovation. In contrast, when a science-based, clean follow-on biologics approval pathway is adopted, it will open the door to meaningful biologics competition and will spark tremendous market incentives for true innovation and better medicines. A sound approval pathway will lead to more competition and true innovation.

5. If a follow-on biologics pathway was created without ample incentives for innovators to continue to innovate, what would the effect be for future research, current clinical programs, and universities?

   Response – 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 follow on biologic approval pathway would not have a similar effect if adopted in the mold of Hatch-Waxman. On the other hand, a pathway strewn with unnecessary obstacles would lead to less innovation, no incentive to compete in the biologics arena, and could harm academic research as our answer to #4 above demonstrates.

European Model (abbreviated approval pathway)

1. The European Union (EU) regulatory system for biosimilars requires the development of product-specific guidances which detail the standard for approval that would need to be met by a biosimilar in a defined product class. Do you think these guidances would provide similar benefits to industry, healthcare providers, and patients in the U.S.?

   Response – The EU system is not comparable to the U.S. drug approval system. Thus, what was adopted in the EU cannot be picked up and dropped into the U.S. system. Under the U.S. system, the issuance of guidance by the FDA prior to FOB application review and approval would merely serve to delay submission or approval of an FOB.

2. Legislation passed by the European Parliament encourages innovation by providing 10 years of market exclusivity, extendable to 11 years for select new indications of use, for innovator biologics, thereby preventing the introduction of FOBs during that period. Should the U.S. be guided by treatment of drugs and biologics in the EU with respect to exclusivity periods?

   Response – Lengthy periods of market exclusivity do not encourage innovation; competition does encourage innovation. We see no reason to change the current market exclusivity provisions that exist in the small molecule market. Also, because the EU has price controls and a more narrow scope of patent protection, any argument for an exclusivity approaching 10 years is indefensible.

3. If the U.S. adopts incentives for innovation in biologics that are substantially less than those afforded in Europe, what could the potential effect be on U.S. competitiveness?

   Response – Lengthy periods of market exclusivity do not encourage innovation; competition encourages innovation. We are unaware of any

evidence to the contrary. Also, as noted earlier, the U.S. pharmaceutical market already accounts for investment through pricing.

4. To what extent do you agree or disagree with the EU's current model when it comes to access to needed biologics, patent protection, patient safety considerations (including interchangeability), and the length of time needed for the approval of a new product? What are the advantages and disadvantages of the EU's model? Are there other models that the U.S. can examine? If yes, what are the strengths and weaknesses of their models?

   Response – A U.S. system should be based on the same fundamental aspects as are embodied by Hatch-Waxman, assuring the safety and efficacy of generic versions and balancing access and innovation. The U.S should adopt a patent process that allows legitimate patents to protect innovation while establishing a process to challenge those patents that are not infringed, not enforceable or are invalid. The latter aspects encourage competition and access to these medicines. Again, it is also important to remember that Europe utilizes price controls. Therefore, considerations for market protection in the EU and the U.S. are markedly different. The U.S. model should account for the dynamics of a free market.

   Regarding safety, FDA should have the flexibility to establish the approval requirements for biogenerics on a case by case basis. As stated by Dr. Janet Woodcock, FDA should make approval determinations based on the available science to assure safety and efficacy. Clinical studies may or may not be necessary depending upon the product. Additionally, interchangeability determinations should be permitted in the U.S. system. Interchangeability should be a scientific decision made by FDA experts.

5. FOBs are now approved in Europe, and FDA has approved a number of follow-on protein products under the FFDCA. Have these shown any problems with respect to safety or efficacy? In what ways are these different from any safety problems seen with brand products?

   Response – To the best of our knowledge, there have been no safety or efficacy issues with the currently approved FOBs in Europe. Additionally, there is no definitive difference in safety for branded products versus FOBs.