Teva Pharmaceuticals Response to the House of Representatives Energy and Commerce Committee, Subcommittee on Health Re: Questions on Generic Biologics 5.02.08

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?

Immunogenicity is the ability of a substance to stimulate the body's immune response. People routinely make antibodies to many different substances and experience no negative effects.

Occasionally biologics can cause patients to develop antibodies to the biologic. In many instances these responses are temporary and patients continue to receive the biologic with no adverse impact.

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?

The requirement for immunogenicity testing should be at the discretion of the FDA. The need for testing of a generic biologic, including immunogenicity studies, should be decided by FDA on a case-by-case basis based on the latest scientific knowledge.

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?

FDA has appropriately exercised its discretion in deciding whether to require immunogenicity testing for manufacturing changes. Immunogenicity testing

after manufacturing changes should not be mandated, but decided on a case-by-case basis.

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?

If two biological products are comparable, they have a comparable structure and biologic activity. Testing the safety and effectiveness of follow-on biologics to their comparator should not include replication of all safety and efficacy studies in all indications.

Under current FDA requirements for approval of generic drug products, when a clinical trial is necessary to show equivalence, only one of potentially several brand-approved indications needs to be evaluated for the generic to be considered equivalent for all uses. There is no reason that this should be any different for follow-on biologics.

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?

FDA has the authority to request post-marketing studies for any product in order to address issues of safety and efficacy. Since safety considerations are always paramount, FDA should have the authority to address safety of the generic biologic in the same manner as set forth under the Food and Drug Administration Amendments Act of 2007.

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?

There should be no statutory requirement for separate and distinct names for generic biologics when FDA determines that there is convincing scientific data that demonstrates that the generic biologic has comparable molecular composition compared to the reference product.

a. What should the standard be for interchangeable FOBs?

Interchangeability standards should be based on molecular characteristics and other scientific evaluations. Interchangeability should be determined on a case-by- case basis considering all essential aspects of the product and the comparability data used in making the determination.

b. What are the advantages and disadvantages of requiring different non-proprietary names, including any affect on patient safety?

There are no advantages.

The disadvantage will be the confusion caused by such a naming strategy, resulting in a concern of difference by patients and physicians.

c. What alternatives are available?

If FDA determines that the generic biologic is comparable to the reference product, then the products are assigned the same INN.

6. 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?

Many biologics have been approved without knowledge of the actual mechanism of action.

There is no scientific justification for the generic biologic to have to prove the mechanism of action where the brand company received approval without having done so.

7. 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?

It is widely known that all biologic products have some degree of variability

batch-to-batch. This variability is controlled by setting product release specifications. These specifications are reviewed by FDA before approval.

8. 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?

Clinical trials should be determined at the discretion of FDA on a case- by- case basis. FDA should be given discretion to determine whether clinical data is appropriate for the approval of a generic biologic.

a. Would not requiring human clinical studies of FOBs result in these products having a more difficult time reaching market acceptance? Why or why not?

Clinical studies by themselves will not create automatic acceptance. Relying on the expertise of FDA will create the needed level of confidence in the healthcare communities.

9. 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?

FDA has reported that a clinical study was required for a 505(b)(2) NDA for calcitonin while no clinical studies were required for a 505(b)(2) NDA for glucagon.

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

a. Have patients experienced any problems?

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

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

We are not aware of any problems experienced with Omnitrope.

We have no access to the information with respect to payers' experiences.

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?

Any new pathway for new highly similar and interchangeable biologics, called "generic biologics", must be available prospectively under the Public Health Service Act. Section 505 has already been interpreted to permit a flexible and shorter pathway for some generic biologics subject to FDA approval. Products already qualifying under the pathway should not be forced to reapply under a new pathway.

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?

Teva is very comfortable with a statutory regime that affords FDA the discretion to decide whether a change to an already-approved biologic requires assessment through a clinical trial. If FDA was capable of making the scientific determination to approve a new medicine as safe and effective, it is equally capable of making the determination relating to whether modifications of that medicine compel clinical trials or not before considering whether to approve the modified medicine. Sometimes FDA does call for such trials, but sometimes it does not. FDA's exercise of its informed case-by-case expertise without artificial restrictions has a positive effect on patient safety.

3. What FDA office should review FOBs?

Staff in the Center for Drug Evaluation and Research with existing responsibility for the class of biologics should perform the review of generic biologics.

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?

The required standard should ensure that an applicant for a generic biologic product provides data establishing that the reference product and the proposed product lack clinically meaningful differences in terms of safety, purity and potency. FDA would apply this standard using its science-based expertise, as it did in approving the reference product initially.

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?

Teva does not believe FDA should be forced to promulgate guidances and regulations before considering generic biologics. FDA should be free to adopt such guidances and rules as it sees fit. But FDA should not be precluded from considering or approving any generic biologic applications because of the absence of any form of guidance or regulations. Requiring FDA to issue guidances prior to submission and/or approval of generic biologic applications would significantly and unnecessarily delay generic competition. In addition, if FDA decides to issue guidances, those guidances will be better informed and workable if developed after FDA has practical experience reviewing generic biologic applications.

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?

User fees should be one element of the funding for a generic biologics program at FDA. It is difficult to assess the precise proportion of the funding that comes from user fees without first knowing the resource needs of the FDA.

Teva would not object to some form of fair and equitable mixed funding approach.

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?

We believe that interchangeability decisions are currently possible for some biologics. As technology progresses, FDA will be able to make interchangeability decisions for a larger number of products.

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

The testing platform for interchangeability will need to depend on the complexity of the product and be determined on a case- by- case basis.

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.

The statute must give FDA the authority to determine interchangeability as technology permits. The best pathway would allow FDA to adapt to and accommodate developments in science as they occur.

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?

The disadvantages are that opponents of generic biologics will inundate FDA with comments in opposition to each guidance published by FDA; the substantial review time by FDA staff to assess each and every comment, and the subsequent time for publishing guidance will take years.

FDA should rely upon its scientific expertise to make interchangeability decisions. FDA may wish to utilize guidances for some products, but the

availability of guidances should not prevent submission and review of generic biologics 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?

FDA will make interchangeability decisions only after it has carefully evaluated the scientific information and determined that the generic biologic is therapeutically equivalent.

The availability of generic biologics will provide lower cost alternatives to brand biologics, which are historically extremely expensive. Affordability is typically associated with better patient access and patient compliance.

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

Interchangeable generic biologics would give pharmacists and doctors the choice of switching from a brand to a more affordable generic equivalent.

Given the need for affordable, safe and effective biopharmaceuticals, it is very important that the FDA be given authority to use its expertise to make critical judgments to determine that two products are interchangeable.

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

The amount of testing will depend on the nature and complexity of the product.

8. 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.

FDA needs to have the authority to determine interchangeability. A case-by- case approach is necessary which allows for product-specific considerations.

9. 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?

If FDA uses its scientific expertise to determine that two biologics are interchangeable, physicians, pharmacists, and patients should feel confident in their use and substitution for the brand product.

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?

The effective patent term necessarily varies from product to product. Teva is aware of no data that analyzes how long, on average, drugs are marketed under patent protection following FDA approval.

Some may cite a July 1998 CBO study as evidence that the average effective patent term for pharmaceuticals is about 12 years. This 10 year old study is not a reliable basis on which to draw a fundamental public policy/competition line that will affect consumer and taxpayer medical costs annually in the tens of billions of dollars, at least. First, the study is outdated and is based only on data from 51 drugs approved between 1992 and 1995. Second, the study does not answer the relevant question: what is the average period for which pharmaceuticals enjoy a patent-based monopoly? Instead, the study calculates an average effective patent term based only on how much time was left on the listed patents when each drug was approved by FDA. It does not analyze when or how soon generics could have entered the market following FDA approval of the branded drug.

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?

Yes, a 5 year period of data exclusivity is a good model for biologic manufacturers. Although we are aware of no study addressing this specific

question, it is clear from the success of both the branded and generic industries over the last 24 years that the balance struck in the Hatch-Waxman was appropriate.

3. Please explain if patents on biotech medicines will provide meaningful protection of intellectual property if a pathway is created to allow for 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 FOB be highly similar to the reference product?

Biologic manufacturers claim they need extra long periods of data exclusivity for biologics because, they allege, patents on biotech medicines are "weak." There is no reliable data to support this remarkable claim. In fact, the available data shows that, biotech patents are normal, not weak. A review of biotech patent cases adjudicated over the last five years confirms that:

o The win-rate in biotech cases is within the normal range for all patents, if not better; and

o The win-rate in biotech cases is within the normal range for all asserted patents in Hatch-Waxman litigations, if not better.

Moreover, on average, there are many more patents relating to any biologic product than to any drug product. These patents claimed a variety of "inventions," including processes for making biologics, purified proteins, amino acid sequences, methods of use, process of manufacture, and formulations. Each claim of each patent presents an independent opportunity to maintain a patent monopoly for biologic medicines.

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?

Patent uncertainty acts as a drag on generic product investment and market introduction. Thus, the legislation should provide a mechanism for the clear and timely resolution of patent disputes but prohibit frivolous suits from restricting access to generic biologics and delaying competition in the marketplace. Such a system should promote informed decisions by generic manufacturers to enter the market for a particular medicine. Moreover, both brands and generics benefit if the "strongest" patents are litigated first and fast.

This goal is best achieved via a voluntary process that is initiated by the generic company with incentives for all parties to come to the table in a timely manner.

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

The reference product sponsor should be required to list all patents it owns or licenses that may be relevant to the reference product. It should also be required to inform all third-party patent holders that it has received a request for a relevant patent list from a generic company.

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?

No. A generic biologics statute should not require FDA to administer patent listing and notification provisions as Hatch-Waxman does. FDA is not well-equipped to carry out these duties nor to police the brand's compliance with its listing obligations. Appropriate notification can be accomplished through an alternative and voluntary process that does not expend FDA resources.

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?

The current framework of the Hatch-Waxman Act provides a well tested, rigorous model for any new legislation regarding generic biologics. Any market exclusivity terms that are longer than the five years provided under Hatch-Waxman would diminish the importance of and reliance upon our patent system. Extended, government-granted, absolute market exclusivity periods would permit the developer of biopharmaceuticals to "double dip" by taking advantage of the absolute market exclusivity provision as well as garnering the fruits of the patent system.

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

Teva is aware of no reliable assessments that have been conducted to answer this question.

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

Exclusivity for modifications to approved products needs to be addressed with great care, guided by experience with the Hatch-Waxman model. Allowing for additional automatic periods of exclusivity for any modification to an approved product would, in effect, provide "innovators" with a potential monopoly in perpetuity by obtaining new biological product licenses for even modest changes to its original product. If the modifications to the approved products are new, nonobvious and useful, "innovators" will be rewarded with strong patents and will not "need" additional and extensive statutory exclusivity.

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

Data and market exclusivity differ from patent protection in that data and market exclusivity are automatic and unchallengeable. Patent protection, on the other hand, is available only for true innovation and can be challenged.

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

There is no legitimate reason to favor the biopharmaceutical industry over all others in terms of providing to them a different period of market exclusivity. Providing enhanced market exclusivity provisions in any generic biologics legislation would, without any doubt, disrupt the delicate balance between fostering biopharmaceutical innovation and consumer accessibility to affordable medicine. See also Response to #2 in Patents section above.

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

To incentivize innovation, industry should be rewarded through the patent system. Patents are granted for innovation and typically provide protection beyond an exclusivity period. Using regulatory exclusivity as a proxy for

patentability holds the risk of allowing small incremental changes to a product to receive years of monopoly protection while ignoring true innovation.

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?

Unless empirical data are produced to show otherwise (and they have not been), current IP protections through 20-year patents and existing exclusivity periods, are adequate to incentivize new drug innovation. These exclusivity periods have proven to be sufficient to incentivize innovation under Hatch-Waxman, and there is nothing to demonstrate that they will not also be sufficient here.

Economic Impact

1. How much savings would a generic biologics pathway create and in what period (taking into account the time it would 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.

A new economic study released in February 2008 by economist Robert Shapiro estimates that potential cost savings generated by generic biologics would total as much as $378 billion over the next 20 years. The study found that generic versions of the top 12 categories of biologic drugs with patents that either have expired or are soon to expire could save Americans $67 billion to $108 billion over 10 years and $236 billion to $378 billion over 20 years. The study concluded that the economic and medical benefits from generic biologics "should be as great or perhaps even greater as those from generic forms of traditional pharmaceuticals." According to a 2007 report from Citizens Against Government Waste, $43.2 billion in economy-wide savings could be realized from generic biologics during the period 2011-2020, and the savings would increase annually from $1.0 billion in 2011 to $6.3 billion in 2020 as more drugs come off-patent. Other studies have produced varying levels of estimated savings, but all agree that the savings are measured in the billions of dollars each year.

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 brand name product, were available, what is your estimate for the cost of the reference product and the follow-on product?

If a workable pathway and patent certainty for biologics is enacted, Teva will commit substantial resources toward providing generic competition for biologics. Numerous studies have estimated the generic discount at 10 to 30 percent below the reference brand price after one generic entrant and up to 40 or 50 percent after multiple generic entrants.

The important point is that any level of savings—even a 10% to 20% reduction in costs—would amount to tens of billions of dollars for consumers and the healthcare system over the next decade. The market for biopharmaceutical medicines is growing at an astonishing rate (more than twice the rate of traditional drugs), and now represents approximately $50 billion in U.S. sales. Annual U.S. sales of biologics are projected to hit $100 billion in three years and account for more than one-fourth of total drug spending (April 26, 2007, Drug Trend Report). More significantly, Medicare spending for bio medicines continues to escalate disproportionately to Medicare funding.

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

A science-based, follow-on biologics pathway would strengthen U.S. economic competitiveness by permitting low cost biologic medicines to reach patients sooner, not later. The pathway will reduce the cost of these medicines for patients and taxpayers as well as businesses. By allowing businesses in all economic sectors to save on otherwise monopolistic biologic medicine prices, the pathway will enable U.S. businesses to use those cost savings for more capital investment, making U.S. businesses more innovative and competitive world-wide.

The pathway will not affect valid and enforceable patent rights in any way. Any legislation should follow the successful Hatch-Waxman model and balance the need to protect intellectual property interests of brand companies against the need for vigorous competition through generic biologic medicines which FDA finds would be safe and effective.

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?

U.S. antitrust statutes are premised on the principle that competition drives innovation, monopolies do not. Patent holders for biologic medicines exercise monopoly power for a specified period of years. 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 will similarly perpetuate brand company monopolies, and create substantial disincentives for innovation. In contrast, when a science-based, generic 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 innovation.

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

No one has proposed a biologics pathway without ample incentives for innovators to continue to innovate. To the contrary, the period of exclusivity provided under the patent laws will incentivize innovation as it has for more than 200 years. To the extent additional incentives are appropriate, then the exclusivity provided under Hatch-Waxman is sufficient. The Hatch-Waxman formula has had a positive effect on pharmaceutical research and development programs throughout the United States. Additionally, there is no reason to believe a generic biologic approval pathway would not have a similar effect if the Hatch-Waxman model is adopted. On the other hand, a pathway strewn with unnecessary obstacles would lead to less innovation as "innovators" would be incentivized to do only the bare minimum required to maintain exclusivity.

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.?

Teva believes mandated EU-style guidances could harm, and would certainly delay, the introduction of new generic biologic medicines as a means of providing lower cost alternatives to branded biologics. FDA should be allowed to issue guidances if FDA finds they would be helpful and in the public interest.

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?

No. The U.S. should not be guided by the EU's system of price controls for medicines. Price controls may inhibit an innovator from receiving what it believes to be a fair return on its investment. To the extent the EU provides for extended monopoly periods of 10 years, it must be seen as a trade-off for price controls. Accordingly, if the EU model is a guide, it would guide the exclusivity period in the 'non-price control' U.S. system toward a level much less than 10 years, just as it is for small molecule drugs.

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?

Grants of statutory monopolies are not incentives to innovate. Just the opposite, monopolists rarely feel the urge to innovate. The U.S. economy would be much more competitive world-wide if the cost of biologic medicines declined in the U.S. to levels driven by competition, not by monopolies. That will only happen when there is a science-based, abbreviated pathway for approval of generic biologic products as safe and effective with corresponding provisions for patent certainty. Then there will be meaningful generic competition in the biologic market and the lowered costs for many biologic medicines will make the U.S. economy much more competitive.

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?

The EU system may work fine for the EU market, but should not be codified here. Teva strongly supports the free market economic environment in the U.S. and looks forward to working to establish a biologic pathway that will fit the pro-competition economic model in the U.S.

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?

Teva is not aware of any problems with brand products other than the absence of meaningful competition and resulting high prices.