January 5, 2009

By Electronic Mail

Federal Trade Commission
Office of the Secretary
Room H-135 (Annex F)
600 Pennsylvania Ave. N.W.
Washington D.C. 20580

Dear Commissioners:

Re: Emerging Health Care and Consumer Issues: Competitive Effects of Follow-On Biologics – FTC Project No. P062105

Mylan is pleased to submit the enclosed brief on competition issues that Congress will confront in developing a biosimilar/biogeneric regulatory pathway. As one of the world's largest generic drug manufacturers, Mylan is devoting substantial resources to biologics development and is delighted that the FTC is thinking about the competition issues likely to arise upon adoption of an abbreviated biologics approval pathway. Mylan would like to take this opportunity to highlight the following key points:

(1) Now is an opportunity to learn from the success of *Hatch-Waxman* and create an even better system for biologics.

(2) Fierce competition will generate savings and foster innovation.

(3) Any effective biosimilars pathway must promote cost-saving generic substitution, not unwarranted generic differentiation.

We discuss each of these points briefly below. Additionally, these issues are addressed in greater detail in our enclosed submission which answers the questions posed by FTC.

1. Learn from the Success of *Hatch-Waxman*

1984's *Hatch-Waxman Act* generated a balance between new drug innovation and affordable access, wherein brand drug manufacturers were given enhanced incentives to develop new drugs and generics were given incentives to be the first to challenge weak or invalid brand patents. Since *Hatch-Waxman*'s enactment, generic utilization in the United States has risen from 19 percent to 67 percent, saving American consumers tens of billions of dollars per year.

Over the years, Congress and the FDA have struggled to preserve *Hatch-Waxman*'s balance, amid changing market conditions and the ever-evolving nature of the *Hatch-Waxman* system. For example, in 2003, Congress plugged a loophole that allowed brands to "evergreen" their patents. In 2007, Congress enacted a provision that prevents brand citizen petitions from unduly delaying generic approvals. Even today, generics have seen the 180-day exclusivity period conferred to them by Congress misappropriated by brands that launch authorized generics in efforts to prevent or delay generic competition.

While we continue to perfect *Hatch-Waxman*, it would be foolish to discard the lessons learned since its introduction. In developing a proposed biosimilar policy for recommendation to Congress, the FTC should use the balance created in *Hatch-Waxman* as a starting point. Where appropriate, its shortcomings – such as the practice of launching an authorized biosimilar upon biosimilar entry – should be fixed. There is no need to reinvent the wheel.

2. Timely and Robust Competition Will Foster Savings and Innovation

The goal of any biosimilar pathway should be to create robust competition within biologics product classes – this will ensure that potential savings from biosimilars are maximized and that biologics innovation remains strong.

The potential for enormous savings is owing to the very high costs of current biologic treatments, which often run in the tens of thousands of dollars for a single patient. Whereas now, these treatments are often accompanied by co-pays in the thousands of dollars, biosimilars could bring such treatments within the realms of affordability for patients. Increased direct competition will certainly result in lower prices – the Congressional Budget Office recently noted that three-quarters of Americans' $40 billion annual spending on biologics is for brand-name products that could potentially lose patent protection over the next 10 years, estimating savings between $9.2 billion and $12 billion.

In addition to generating substantial savings, an intelligent abbreviated biologics pathway will also foster innovation. Competition, not protection, is the true source of innovation, and overextending monopoly protection can be counterproductive. Nevertheless, there appears to be great concern among current biologics manufacturers that additional incentives, in the form of market exclusivities or other barriers to generic entry, may be necessary to stimulate new biologic innovation. As timely biosimilar entry is critical to stimulating the development of new biologics, efforts to increase the time period of exclusivity beyond that already afforded should be evaluated by lawmakers with strict scrutiny.

3. Substitutable Biologics, Not "Me-Too" Biologics

Congress is at a crossroads, and must decide whether to create an abbreviated biologics pathway that promotes incentives for biosimilar substitution or incentives for biosimilar differentiation. Only a system promoting biosimilar substitution will yield the savings that the Obama administration needs to finance meaningful health care reform.

Already, there is competition within therapeutic classes in biologics markets. However, the companies selling these products do not compete on the basis of price. Rather, they spend enormous amounts on marketing to differentiate their products from one another, even where

the molecules are identical or nearly identical. Congress must choose to either perpetuate this state of affairs, or remedy it.

Mylan supports an integrated system which creates abbreviated pathways for both comparability and interchangeability, leaving FDA to determine, based on prevailing science, the standards to be met for any given submission. At the same time, parallel mechanisms are necessary to ensure that, at every level, health decision-makers are encouraged to prescribe lower-cost comparable and/or interchangeable products where medically appropriate. This would include such measures as giving biosimilars the same reimbursement code as their brand name counterparts and preempting state efforts to outlaw biosimilar/biogeneric substitution.

By promoting substitution of biosimilars where appropriate, Congress can generate market dynamics that encourage price-based competition, thereby increasing access and affordability for Americans.

* * *

We understand that the scientific, regulatory and economic issues relating to generic competition in biologics markets are complex, and generate considerable attention from a broad array of stakeholders. We applaud the FTC's interest in this area, and would welcome any opportunity to provide future comments on this very important topic.

Yours very truly,

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COMPETITION ISSUES INVOLVING FOLLOW-ON BIOLOGIC DRUGS
COMMENTS OF MYLAN INC.

PART I:
REGULATORY EXCLUSIVITIES AND FOLLOW-ON BIOLOGIC DRUG COMPETITION

1. Expected Competitive Effects

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?

The competitive effects of biosimilar competition will depend greatly on whether incentives exist for biosimilar substitution without unnecessary barriers to market uptake.

The competitive effects of the introduction of biosimilars in the United States will include:

- increased treatment affordability;
- broader access to treatment; and
- substantial cost savings for consumers and taxpayers.

Twenty-five years of experience with small-molecule generics approved under the *Hatch-Waxman Act*'s abbreviated drug approval pathways has yielded enormous savings for consumers, and has seen generic utilization increase from 19% to 67%, largely due to the $85 average savings (and growing) experienced by consumers every time they purchase a generic prescription rather than a brand prescription.[1] This translates to annual savings in the tens of billions of dollars.[2] The prospects for additional savings on biologics, whose U.S. sales exceeded $40 billion in 2007, are similarly impressive – the Congressional Budget Office recently noted that three-quarters of spending on biologics is for brand-name products that could potentially lose patent protection over the next 10 years, and estimated savings from biosimilars during that period between $9.2 billion and $12 billion.[3]

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[1] NACDS: www.nacds.org/wmspage.cfm?parm1=507#pharmpricing.

[2] In the Congressional Budget Office's 1998 report "How Increased Competition from Generic Drugs Has Affected Prices", the CBO estimated that by substituting generic for brand drugs, purchasers saved roughly $8 billion to $10 billion in 1994 (at retail prices and including only sales through pharmacies). Generic utilization has climbed from about 43% in 1996 to 67% in 2007, suggesting even greater savings.

[3] Congressional Budget Office, "Budget Options: Health Care – Volume I" (December 2008) at 126. Available online: http://www.cbo.gov/ftpdocs/99xx/doc9925/12-18-HealthOptions.pdf.

For small-molecule drugs, abnormal savings have results from reductions of upwards of 80 percent of the brand price within months of generic entry. The regulatory complexity and manufacturing requirements associated with biosimilars will probably prevent a similar percentage price reduction, but per-prescription savings for biosimilars will far exceed the possible savings from small-molecule drugs.

The potential for enormous savings is owing to the astronomically high costs of current biologic treatments. The annual costs of several leading biologics run in the tens of thousands of dollars. Whereas now, these treatments are often accompanied by co-pays in the thousands of dollars[4], biosimilars could bring such treatments within the realms of affordability for patients. Increased competition will certainly result in lower prices, and price erosion at any level would positively affect payers.

The high cost of biologics threatens not only affordability but also basic access to treatment. As biologics sales volumes continue to grow, with one out of eight prescriptions now being written for a biologic[5], patients in the United States are increasingly foregoing costly medical treatment.[6] In 2007, 45.7 million Americans did not have health insurance coverage[7], and patients with chronic conditions facing medical bill problems were shown to be four to five times as likely to forgo or delay care based of cost concerns as those reporting no cost concerns.[8] Increasing biologics co-pays for the insured threaten to reduce access even further. Competitive markets for existing biologics are essential to generating increased biologics access for patients.

With the wrong approval pathway for biosimilars, however, increased access and affordability could be undermined. For example, biosimilar competition will be unduly prevented if innovators are given the opportunity to extend their mature monopolies beyond the life of their patent thickets. Care must be taken to ensure that the adopted pathway does not stymie competition.

Although Mylan is not aware of studies analyzing how competition has developed between referenced and follow-on products in European markets, there are lessons to be learned from the European experience. There are significant structural impediments to rapid market penetration in the EU, including undue no-substitution rules for biologics in individual EU markets. Fortunately, and encouragingly for the United States, the first biosimilars launched in the EU are gaining significant and growing market shares, thus providing consumers with significant savings.

Mylan would strongly caution lawmakers to be clear on the pathway it seeks to create. Will it be a "generic" pathway like that created under *Hatch-Waxman*? Or,

[4] G. Kolata, "Co-Payments Soar for Drugs With High Prices", *New York Times* (April 14, 2008).
[5] Visiongain, "The Global Biotech Report 2006: The rise of the Biotech blockbusters" (September 2006).
[6] V. Culliver, "22% of Americans surveyed cut visits to doctor", *San Francisco Chronicle* (August 13, 2008).
[7] U.S. Census Bureau, "Income, Poverty, and Health Insurance Coverage in the United States: 2007", Report No. P60-235 (August 2008). Available online: http://www.census.gov/hhes/www/hlthins/hlthin07.html.
[8] Ha T. Tu, "Rising Health Costs, Medical Debt and Chronic Conditions", Center for Studying Health System Change Issue Brief No. 88 (September 2004). Available online: http://hschange.org/CONTENT/706/.

will it be a "me-too" pathway that places a premium on marketing expenditure by large companies? Already, biotech companies have made slight changes to their existing drugs, e.g. by adding sugars to improve uptake, in order to revitalize their product lines without starting from scratch. There is no need to provide further incentives for such incremental innovation that does not generate meaningful cost savings. Rather, the goal of any biosimilar pathway should be to create robust competition within the product class – only then may the potential savings from biosimilars be fully realized.

2. Interchangeability

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?

Interchangeability is a prerequisite for robust competition in biologics markets. Competing biosimilars that are designated as interchangeable can be anticipated to achieve more rapid and ultimately more substantial market shares. Any forward-looking legislative solution should include a flexible interchangeability pathway that evolves as the science evolves.

Only a workable regulatory pathway that allows companies to achieve interchangeability designations for their products would provide lower-cost reimbursement options to health plans, the government and other third-party payers. Interchangeable biologics would enable direct, head-to-head competition based on price, by eliminating the effects of advertising and promotion in markets that require substitution of a lower-cost interchangeable product. Existing biologics would thus lose their monopoly status and be forced to operate under normal market conditions, with prices reflecting costs at a normal rate of return that accounts for the biosimilar's R&D investment.

Interchangeability of biologics has been established scientifically, and the FDA has already made interchangeability determinations for several *Public Health Services Act* (PHSA) biologics.

Mylan supports a process for achieving interchangeability involving two decision steps:

(i) **Comparability** - In order to be approved, the sponsor of a biosimilar must demonstrate that it is comparable to a reference biologic (licensed under the PHS Act) – this would be similar to the well-established comparability standard as defined in ICH Q5E, and would lead to regulatory approval of the comparable product; and

(ii) **Case-By-Case Interchangeability –** The decision whether to designate a product as interchangeable would be within the scientific discretion of the FDA, based on the information leading to the comparability determination, and with the possibility (but not in all cases) that the product would be required to meet additional scientific criteria. This would assure a science-based and data-driven process.

The impact of authorized biosimilars on competition is unclear; however, there could be a potential anti-competitive impact on the market depending on the approval pathway adopted. Authorized biosimilars could serve as a disincentive for some companies to invest in biosimilar development programs, resulting in a reduced level of competition in the marketplace.

Specifically, if biosimilar entrants are forced to share information about their potential entry dates with innovators, then innovators may be able to cut deeply into their markets by launching an authorized biosimilar exactly when the true biosimilar expects to recoup its R&D costs. If a patent notification system is implemented which requires the true biosimilar to disclose their competitive process trade secrets, then the innovator could couple an authorized biosimilar (or the threat to launch one) with a very specific citizen's petition to prevent true biosimilar launch. Particularly where an innovator and true biosimilar are embroiled in patent litigation, the threat of an authorized biosimilar would loom very large in such circumstances and could have the effect of delaying or preventing biosimilar entry.

3. Agreements Between Brands and Biosimilars

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?

In Mylan's view, the possibility that existing biologics manufacturers will enter into agreements with biosimilar entrants does not raise any apparent competitive concerns necessitating additional legislative or regulatory action.

4. Effects on New Biologic Innovation

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?

From an innovation perspective, it is in the best interests of patients, taxpayers, healthcare providers and the government that lower-cost generic versions of

medicines are allowed to come to market expeditiously. Competition drives innovation, it does not hinder it.

The market experience with non-biologic generics provides insight into the expected innovation that will be driven by biosimilars. In his September 2008 study, "Stimulating Innovation in the Biologics Industry", Boston University professor Laurence Kotlikoff showed that *Hatch-Waxman* positively influenced research and development, finding as follows:

> "Numerous papers in the economics literature on invention and monopoly protection stress that competition, not protection, is the true source of innovation and that overextending monopoly protection can be counterproductive. ...
>
> Hatch-Waxman's success did not come at the price of innovation. On the contrary, the legislation appears to have accelerated innovation."[9]

Professor Kotlikoff concluded that with proper incentives and reasonable exclusivity, competition from biosimilars should be expected to spur innovation the same way as chemical drugs did under Hatch-Waxman. Professor Kotlikoff is not alone in his observation that generic competition drives innovation. Among others, Scott Gottlieb, former FDA Deputy Commissioner for Medical and Scientific Affairs, has said that legislation to expose biologics to competition would unleash innovation and "accelerate development of improved products, not just lower cost."[10]

If any incentives are given by Congress to reward innovators for new biologics, then it is imperative that (a) the reward not be excessive – as these companies already benefit from lucrative patents, and (b) the reward preserve incentives for fierce competition for existing drugs whose patents have expired or are invalid. A regulatory pathway that unduly preserves monopoly-level prices in the marketplace should be avoided. Above all, it must be remembered that the best incentive to innovate is healthy competition.

5. Medicare Reimbursement

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

[9] L. Kotlikoff, "Stimulation Innovation in the Biologics Industry: A Balanced Approach to Marketing Exclusivity" (September 2008) at pages 1 and 10. Available online: people.bu.edu/kotlikoff/New%20Kotlikoff%20Web%20Page/Kotlikoff_Innovation_in_Biologics21.pdf.
[10] S. Gottlieb, "Biologics Legislation Will Speed Progress" (April 16, 2007). Available online: http://www.aei.org/publications/filter.all,pubID.25967/pub_detail.asp.

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?

In order for taxpayers to achieve the savings that they should obtain from generic competition, Medicare reimbursement of these products will need to be modified to ensure that the system is not inadvertently encouraged to utilize brands over biosimilars. The statutory scheme as it exists within Medicare Part B today does not give providers the same incentives to use biosimilar drugs, and this will need to be changed in any smart biologics legislation.

One measure which could speed the uptake of biosimilars would be to give the same reimbursement code for biosimilars as their brand name counterparts. The Congressional Budget Office has estimated that such a measure would increase the savings from biosimilars by 30 percent for the Federal government's mandatory health care programs over ten years, representing several billions of dollars.[11]

Further, to ensure that the impact of biosimilar legislation is realized nationwide, Congress should preempt states' efforts to enact no-substitution laws targeted at expected biosimilar drugs. Even in spite of an FDA determination of comparability, and in some cases interchangeability, some states may choose to prevent biosimilar substitution on their formularies – much the same way as health plans used to perceive small-molecule bioequivalent generics as inferior. To avoid such measures, Congress should either preempt them, or if that is not feasible, then provide incentives for states to promote biosimilar substitution, taking into account the two-tiered nature of a comparability/interchangeability regime.

6. Biologics Patent Portfolios

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

Biologic products typically have more and broader patents protecting them than chemical drugs. Due to their inherent nature, biologics patent estates tend to include more process patents compared to small-molecule drugs.

Each patent – whether large-molecule or small-molecule – offers 20 years of monopoly protection, regardless of the length of any parallel exclusivity period granted. Additionally, under *Hatch-Waxman*, biologics are eligible for a patent term restoration of up to five years. As a result, valid and enforceable biotech patents offer good and sufficient intellectual property protection.

Nevertheless, even though clear examples show that biologics are protected robustly by patents, such as Amgen's successful patent infringement lawsuit preventing

[11] C. Dombrowski, "Follow-On Biologics Coding Tweaks Could Raise Savings By 30% - CBO," *The Pink Sheet*, vol. 70, no. 51 at page 23 (December 22, 2008).

Roche from launching its anemia drug Mircera®, some innovators claim that patents are not enough to guarantee protection of biotech drugs (since biologic patents primarily claim a process rather than a chemical entity). It has become almost common wisdom that some form of additional exclusivity is needed in addition to patents to ensure proper protection for brand biologics. Given the past success of patents in the biotech sphere in protecting decades-old biotech franchises, these claims by innovators should be evaluated by lawmakers with strict scrutiny.

7. Existing Innovator Exclusivities

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?

The balance generated by *Hatch-Waxman* has been extremely successful for brands and generics alike, and is an appropriate starting point in the creation of a workable abbreviated biosimilars pathway. *Hatch-Waxman* strikes a reasonable balance between market incentives and competition, and provides timely and affordable access to drugs for Americans.

We are unaware of any valid assessments supporting the need for a brand exclusivity period different from that provided under *Hatch-Waxman*. However, we have reviewed and find persuasive the recent work of Professor Kotlikoff, in which he found as follows:[12]

- Hatch-Waxman is likely the best model for an approval pathway for biosimilars, as it would both spur innovation and allow competition in the marketplace.

- There are no meaningful differences between the pharmaceutical industry and the biotech industry to justify deviating from the *Hatch-Waxman* model.

- Compared with pharmaceuticals, biologics are more costly to produce. However, their reward is also considerably higher. Compared to chemical drugs, biologics have a lower invention cost to reward ratio.

- There are no justifiable reasons why a biologics pathway should be treated differently than for chemical drugs because not only is the biotech industry not riskier than the pharmaceutical industry, but the opposite is true.

- When it comes to non-diversifiable risk, the biotech industry is riskier than most, but not by much. Furthermore, a quarter of U.S. industries are riskier than biotech, but none of these garner longer monopoly protection.

[12] *Kotlikoff,* see footnote 9.

Given the findings of Dr. Kotlikoff in view of the success of *Hatch-Waxman*, the FTC should only depart from *Hatch-Waxman*'s cocktail of incentives in clearly appropriate circumstances. No such circumstances exist to justify a departure in respect of brand regulatory exclusivities.

8. Additional Innovator Exclusivity

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?

As mentioned earlier in our responses to the previous two questions, no objective assessments support the need for an exclusivity period different from what is provided in *Hatch-Waxman*. No new exclusivity incentives are necessary, and they should not be handed out lightly as political bargaining chips.

The factors that lawmakers should consider in setting the optimal length of regulatory exclusivity include:

- Providing incentives for innovation and competition; and
- Avoiding brand evergreening.

Professor Kotlikoff demonstrates that the *Hatch-Waxman* model provides the needed balance, and that biotech companies should not receive anything above and beyond the exclusivities afforded under *Hatch-Waxman*. *Hatch-Waxman* offers five years of exclusivity generally, with four years of data exclusivity followed by one year of approval exclusivity if an applicant files a patent challenge in the fourth year.

Any exclusivity that extends beyond that in *Hatch-Waxman* will not only harm short-term competition but also harm innovation in the short- and long-runs. As noted by Professor Kotlikoff, referring to Kenneth Arrow's seminal work on invention economics, "the incentive to invest is less under monopolistic conditions than under competitive conditions … [because] bringing new products to the market undercuts a monopolist's revenues on his existing products."[13] If exclusivity is excessive, we can expect brand companies to routinely make relatively minor changes to their existing products to extend their monopolies in any way possible.

9. European Data Exclusivity

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?

[13] *Kotlikoff,* see footnote 9 at page 5, citing Arrow, Kenneth J., "Economic Welfare and the Allocation of Resources for Invention," Rand Corporation working paper P-1856-RC, December 15, 1959.

A direct comparison between Europe and the United States is difficult, because the EU has a reference pricing system that changes the market dynamics for any new biologic. Nevertheless, Europe has pioneered the safe and effective abbreviated approval of biosimilars by creating a formal and specific pathway. The EU recognized that it was not necessary to depart from the regulatory exclusivity regime that applied to small molecule drugs in Europe, and so the European Medicines Evaluation Agency (EMEA) provides for one regulatory exclusivity period across the board. Mylan supports such a consistent approach.

10. Biosimilar Exclusivity for Development

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?

The 180 days afforded generics under *Hatch-Waxman* has been a critical incentive for generic companies to undertake the risk that comes with challenging brand patents. A short marketing exclusivity period, as under *Hatch-Waxman*, would provide an incentive to enter the nascent (and therefore highly risky) biosimilar market.

Mylan supports an exclusivity period as found in H.R. 1038, which provides exclusivity for the first interchangeable biosimilar, but such exclusivity does not prevent the immediate approval of a non-interchangeable, but comparable, biosimilar. It also provides exclusivity to the first company to obtain an interchangeability approval from FDA, rather than to the first company to file an application for such an approval (as is the case under *Hatch-Waxman*).

PART II:
PATENT DISPUTE RESOLUTION ISSUES

1. Regulatory Patent Linkage

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

Patent uncertainty is a critical barrier to biosimilar entry, and the greater this uncertainty, the more biosimilar product investment and market introduction will be prevented. Mylan supports the creation of a fair and effective patent dispute resolution mechanism.

<u>It is imperative that patent issues be resolved as quickly as possible to expedite biosimilar market entry and increase competition.</u> If a patent ruling cannot be obtained prior to FDA approval, biosimilar entrants will be discouraged from launching "at risk" of potential massive damages given the significant costs of

branded biologic drugs. Thus, biosimilar drug legislation should provide a rock-solid pathway for generics to get into court as early as possible upon filing a biosimilar application. As provided in question 3 below, biosimilar legislation should provide a clear statutory right of action for biosimilar applicants to obtain a declaratory judgment of invalidity or noninfringement upon the filing of an abbreviated BLA, irrespective of whether the brand has filed suit on any of its patents.

Moreover, patent resolution under any biosimilars pathway should be initiated by the biosimilar entrant, affording the biosimilar entrant the opportunity to invite patent certainty on its own terms before launching a product (after which the brand would have normal patent law remedies available). Any alternative solution which allows the brand company to sue on any patent it chooses prior to biosimilar launch would encourage frivolous suits intended to delay the biosimilar company's ability to launch its product or to obtain patent certainty in respect of all potentially relevant patents. It could also invite gaming by the brand company, e.g. by launching an authorized biosimilar product to compete with the true biosimilar on or before the known biosimilar entry date.

2. Length of Biosimilar Approval Process

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

If supported by user fees, Mylan expects that the biosimilar approval process will be similar to the process for proprietary small molecule approvals. We believe that FDA will be able to review and license biosimilars within the period provided for all other products – currently 10 months under the *Food and Drug Administration Amendments Act of 2007* (FDAAA).

3. Biologics Patent Litigation Dynamics

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

Mylan does not believe that there is any relevant difference between patent portfolios for small molecule drugs and biologics that might affect patent litigation. Thus, the length of patent litigation should be similar.

The most important factor in how long a brand/generic biologic patent case will take likely will be the patent dispute resolution mechanism that Congress enacts as part of a follow-on biologic approval pathway. Mylan endorses a system like that proposed in H.R. 1038, the *Access to Life-Saving Medicine Act*. The notification system set out in H.R. 1038 provides an opportunity for brands to allege patent infringement against biosimilar entrants, but also provides incentives for timely management of the litigation by not offering an automatic stay against regulatory approval of the biosimilar. This ensures expeditious patent dispute resolution and

thus expedited generic marketing, while still respecting legitimate patent rights under traditional patent law.

Because of the voluminous amount of process and manufacturing patents that can be obtained by a brand biologic company, Mylan fears a significant delay in access to biosimilar products if generic applicants are required to challenge every patent prior to market entry. If a 30-month stay is proposed, then Mylan supports a patent listing system that requires the brand company to identify only the most pertinent patents, and the listing of a patent should be limited to patents that cover the use of the product. Moreover, such listing should be accompanied by a strong certification subject to verification by the patent holder and the marketing authorization holder listing the patent. To minimize the potential for abuse, generic applicants should have the ability to file an independent claim challenging the listing of any patent irrespective of the originator or patent holder filing a patent infringement suit.

4. Timing of Patent Issue Resolution

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

Patent uncertainty is problematic, as it inhibits product investment and timely marketing; assuming no undue incentives to delay biosimilar entry, the timely resolution of potential disputes benefits all parties.

Biosimilar drug legislation should provide a mechanism for timely resolution of patent disputes that does not unduly delay biosimilar entry. This could be achieved through a voluntary process that is initiated by the generic company, such as the one proposed in H.R. 1038 (discussed in our answer to question 3, above).

5. Declaratory Judgment Availability

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

It is critical that the generic companies have an effective and reliable mechanism for litigating all relevant patents. In light of the courts' reluctance to allow a declaratory judgment action when the brand company has not brought suit, biosimilar legislation should provide a clear statutory right of action for biosimilar applicants to obtain a declaratory judgment of invalidity or noninfringement upon the filing of an abbreviated BLA, irrespective of whether the brand has filed suit on any of its patents.

6. Biosimilar Exclusivity for Patent Challenges

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

It should be expected that the brand biologics patentees will seek to enforce their patents, even if they are weak or invalid, as has been seen under *Hatch-Waxman*. Biosimilar entrants should have some incentive to shoulder the burdens, risks and expenses that come with patent cases, as their success under a rational biosimilars regime will lead to tremendous cost savings for payers and patients.

As commented above, Mylan supports an exclusivity period as found in H.R. 1038, which provides exclusivity for the first interchangeable biosimilar, but such exclusivity does not prevent the immediate approval of a non-interchangeable, but comparable, biosimilar. It also provides exclusivity to the first company to obtain an interchangeability approval from FDA, rather than to the first company to file an application for such an approval (as is the case under *Hatch-Waxman*).

The 180-day exclusivity period under *Hatch-Waxman* was created to encourage generic drug applicants to be the first to challenge the brand's patents and remove patent barriers to generic approval. The first-to-file *Hatch-Waxman* framework has proven to be an effective reward for generic companies, where it has operated properly, resulting in capital for generic companies to develop additional products and pursue other patent challenges.

The availability of exclusivity is even more important for biosimilar applicants who already face a high barrier to entry in the biologic marketplace as a result of the considerable costs to develop and manufacture biologics. As the FTC has itself recognized, "only a few of the biggest generic firms will be able to afford the huge investments needed to manufacture generic biologics." [14] Challenging biologics patents will likely involve greater litigation costs and risks than small molecule patent challenges (i.e., biologics involve more process patents which will require more experts in litigation; monetary damages against generic applicants could result in unprecedented amounts, given the high costs of branded biologic products, etc). These barriers underscore the need to offer generic exclusivity in order to encourage such applications and patent challenges.

7. Gaming Possibilities

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

[14] Remarks of Commissioner Pamela Jones Harbour, ABA Sections of Antitrust and Intellectual Property Law Conference, San Francisco, CA (June 14, 2007). Available online: http://www.ftc.gov/speeches/harbour/070614genbio.pdf

for the improper use of citizen petitions to delay approval of follow-on biologic applications?

After 25 years of *Hatch-Waxman*, it is clear that a biosimilars bill containing unnecessary barriers will be utilized be the brand industry to delay biosimilar entry. However, as long as straightforward legislation is adopted which delegates approval decisions to the FDA's scientific discretion in a transparent fashion, such gaming may be minimized.

Over the years, Congress and the FDA have struggled to preserve Hatch-Waxman's balance, amid changing market conditions and ever-evolving manipulation of the system. For example, in 2003, Congress plugged a loophole that allowed brands to "evergreen" their patents. In 2007, Congress enacted a provision that prevents brand citizen petitions from unduly delaying generic approvals. Even today, generics have seen the 180-day exclusivity period conferred to them by Congress hijacked by brands that launch authorized generics in efforts to prevent or delay generic competition.

Learning from *Hatch-Waxman*, we can expect that if brand companies receive long periods of exclusivity, they will find ways to manipulate the process (e.g., by shifting the market from one brand product to the next version of the same brand product) such that consumers likely will receive little benefit from the introduction of biosimilar products. In that case, generic companies will have little incentive to develop biosimilars. We have also learned that generic notification to brands of their entry dates has lead to the timed marketing of authorized generics.

As is specified for small-molecule drugs under FDAAA, citizen petitions should not be permitted to unduly delay approval of biosimilars, and consideration of a citizen petition should be separate and apart from review and approval of a biosimilar application. A provision preventing delaying citizen petitions is contained within H.R. 1038, and is an essential component of any biosimilars legislation.

Ultimately, approval decisions relating to biologics must be made transparently by FDA and guided by science as it evolves, and FDA should not be burdened with the responsibility of handling patent disputes as well. As long as these guiding principles are adhered to, neither brands nor biosimilars will be in a position to systematically game the new biosimilars approval pathway.

8. Patent Settlements

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

It is reasonable to assume that some brand/biosimilar patent litigation cases will conclude with a settlement. Having a broad range of settlement options is critical to resolving any litigation, but is particularly important in complex patent cases. Given the multitude of issues at play in these litigations, settlements are frequently the more efficient and pro-competitive solution.

Mylan recognizes that in some markets, a settlement preventing entry by a biosimilar applicant could possibly perpetuate market power by the brand outside the exclusionary zone of its patents. For that reason, Mylan recommends that settlement participants be required to submit their agreements to FTC and DOJ for review under the antitrust laws, as is required under the 2003 *Medicare Modernization Act* amendments to *Hatch-Waxman*. This would allow FTC and DOJ the opportunity to conduct an antitrust review. Additionally, Mylan recommends measures that would provide FTC and DOJ with a reasonable number of days to review such agreement. If the FTC or DOJ do not respond within this time period, such agreement should be deemed approved by the agencies.