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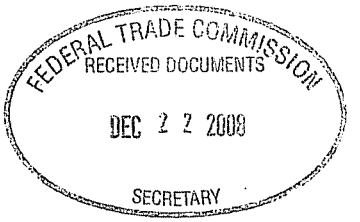

December 19, 2008

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

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

Dear Federal Trade Commission:

Eli Lilly and Company ("Lilly") welcomes the opportunity to comment on matters discussed at the Federal Trade Commission's November 21, 2008, workshop, Competition Issues Involving Follow-On Biologic Drugs. Lilly is one of the largest producers of recombinant DNA derived biologic products in the world. Lilly, in conjunction with our collaboration partners at Genentech, developed and launched the world's first recombinantly-produced human insulin product, Humulin®, in 1982. Since then, Lilly has gone on to develop and launch numerous products manufactured via recombinant DNA technology, including Humatrope® (human growth hormone), Xigris® (activated human protein C), Forteo® (an analog of human parathyroid hormone) and Humalog®, the world's first insulin analog molecule. Lilly currently has nearly twenty (20) biological agents in its pipeline, including molecules for the treatment of diabetes, obesity, oncology, atherosclerosis and osteoporosis.

Lilly's comments focus on the expected nature of competition among innovator and follow-on products, the impact of a follow-on pathway on biologic product development and the critical role of exclusivity in shaping development and marketing of these products. These comments are organized to correspond to certain questions provided by the FTC in advance of the workshop.

Lilly's Response to Designated Questions from the FTC

4. *How would the prospect of competition from follow-on biologic drugs influence research and development for new biologic drugs, improvements to existing biologic drugs, and the timing and rollout of new and/or improved biologic drugs? Does*

the market experience with non-biologic generic pharmaceutical drug products provide insights into these issues?

The prospect of competition from follow-on biologic drugs has already impacted the research and development of many new biologic drugs within Lilly's research component. Appropriate research investments require a level of certainty that has been clouded by the recent debates and the introduction of several disparate bills in Congress. No financially responsible organization can afford to invest the hundreds of millions of dollars[1] required to bring a new biologic drug to the market without having some assurance of a reasonable return on that investment. When weighing the value a new biologic molecule may bring to the pipeline, we remain uncertain about how quickly a future follow-on of our own product may arrive on the market. This uncertainty leads us and other biopharmaceutical firms to turn away from some of the best potential drug products and instead concentrate our efforts on those products with the highest potential for return on investment. In short, rather than developing the best drugs, we are unfortunately required to develop only the drugs with the best patents.

Lilly's market experience with non-biologic pharmaceutical drug products informs these decisions. Under the terms of the Hatch-Waxman Act, generic drug manufacturers are allowed to file Abbreviated New Drug Applications, combined with Paragraph IV patent challenges, a mere four (4) years after the launch of the referenced Lilly drug product. In our experience, every non-recombinantly produced drug product sold by Lilly has received a Paragraph IV certification at or about the expiration of this four year moratorium period. In some instances, more than ten (10) generic firms arrive to make such patent challenges. This litigation-encouraging statutory scheme, in conjunction with the bounty of generic exclusivity it places on the patent estate of the proprietor, adds enormous cost, risk and uncertainty to the already risky business of discovering and developing drug products. Lilly expends tens of millions of dollars a year defending its products from such speculative patent challenges. The toll of industry-wide patent litigation costs and the risk and uncertainty that this litigation brings hinders the ability of research-based firms to develop new treatments and cures. Because it is unclear what statutory scheme will be enacted to promote follow-on biologics, and whether such a statutory framework will encourage extensive and expensive patent litigation, Lilly has been reluctant to make certain investments in our biotech drug pipeline.

Another aspect of the Hatch-Waxman Act that could benefit from legislative attention is the strict limitation on Patent Term Restoration available under the Act. The term of restoration available is the shorter of fourteen years (14) total patent term available after product launch or five (5) years of additional term if the pre-existing patent has less than nine years left on its normal term. When the Act was first passed in 1984, the United States provided a seventeen (17) year patent term measured from the date of patent grant. When the United States joined the World Trade Organization and became a signatory of the TRIPs Agreement in 1995, the term of all subsequently filed patents changed to a period of twenty (20) years from the date of filing the initial patent application. Many drugs now being developed for first launch rou-

[1] One recent study indicates that the cost to bring a new molecular entity to the market is $1.2 billion. DiMasi, JA and Grabowski, HG "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics* 469-479 (June 2007).

tinely have less than nine (9) years left available from their key patent terms since these patent applications were filed post-TRIPs. Thus most of the patent term has expired prior to launch, leading to key patent protection that last far less than the fourteen year cap originally thought appropriate under the Hatch-Waxman Act. This, coupled with the extensive requirements in clinical testing and approval for new chemical entities, threatens the sustainability of the investment model upon which the pharmaceutical and biotech industries were founded.[2] The five year cap on Patent Term Restoration currently set forth in the Hatch-Waxman Act should be revisited and removed, allowing all new chemical entity patents to earn a fourteen year restoration period.

7. *Are the regulatory exclusivities currently provided to pharmaceutical 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 current regulatory exclusivities provided under the FDCA are inappropriately short for both small molecule and biologic drug products. The short four year moratorium period, coupled with the bounty placed on patents arising from the 180-day generic drug marketing exclusivity, requires early and speculative patent litigation that brings risk to even the most long-lived patent portfolios. In the current litigation environment, any patent, no matter how strong, can be challenged and perhaps lost due to the incongruities of the system. If even the best case can be lost 10% of the time, and all products are litigated four years post launch, it should be no surprise that products are placed in the pharmaceutical pipeline with an over-emphasis on patent strength. The public would be far better served if pharmaceutical pipelines were filled with products that best protect and preserve public health, regardless of the strengths or weaknesses of the patents covering those products.

Lilly believes that the appropriate level of data protection for biologic drugs should be at least fourteen (14) years. Professor Grabowski of Duke University has published a study indicating that the proper range of exclusivity for biologic drugs falls between 12.9 years and 16.2 years.[3] Legislation proposed in the 110th Congress set forth ranges of Data Protection between zero (0) and fourteen (14) years. The uncertainty of the direction of these legislative initiatives prevents many biopharmaceutical firms from making the best decisions about where to target their research efforts.

To provide certainty to both innovators and follow-on manufacturers, encourage investment in the best medicines rather than the medicines with the best patent estates and to hopefully avoid lengthy, expensive and risky patent litigation arising from any future follow-on biologic legislation, Lilly proposes an alternative plan. Lilly believes that a regulatory framework can be constructed that provides a proprietor with reasonable certainty concerning expensive and

[2] For discussion new drug approvals over the last decade *see*, Hughes, B "2007 FDA Drug Approvals: a Year of Flux" Nature Reviews Drug Discovery 7: 107-109 (February 2008) available at http://www.nature.com/nrd/journal/v7/n2/full/nrd2514.html.

[3] Grabowski, HG "Data Exclusivity for New Biological Entities," Duke University Department of Economics working paper (June 2007), available at http://www.econ.duke/Papers/PDF/DataExclusivityWorkingPaper.pdf.

risky research investments and provides certainty for development and market entry of follow-on products. Specifically, a company that owns the Biological License Application (BLA) for a product should be allowed to choose to either a) enforce its patent estate against any follow-on manufacturer according to the patent litigation regime set forth in the statute authorizing such follow-on products, or b) decide via a system created by legislation to select a voluntary parallel pathway in which the pioneer firm agrees to accept at least a fourteen (14) year period of data exclusivity in exchange for not enforcing any patents on the initial BLA authorized product after the expiration of the pioneer manufacturer's exclusivity period. The timing of such a choice could come as late as eight years post-product launch, but could also be as early as one year after the launch of the product in the US market.

In some instances, the BLA owner may choose to live with the patent estate if the patents left extant upon product launch are reasonably strong and long lived. As an example, if the product is a monoclonal antibody and the proprietor owns a patent with a specific claim to the antibody product and that patent lasts sufficiently long, then the proprietor can choose to follow the patent enforcement option. This option retains for the proprietor the ability to make investment choices based on understanding of the current patent estate and the inherent risks of patent litigation. If, on the other hand, the proprietor chooses the data exclusivity route, then both the proprietor and any generic follow-on manufacturer are provided certainty for the exact date upon which follow-on competition can begin. A responsible proprietor could have many reasons to select the certainty of an exclusivity-based system over a patent-oriented system. With such options available, proprietors will be far more likely to develop compounds that best meet the needs of the public health system rather than developing compounds that can be best protected by the patent system.

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

Lilly does not believe that any marketing exclusivity period is necessary to encourage companies to develop follow-on biologics and to seek their approval by the FDA. Even without any such follow-on exclusivity, market competition is thriving in the biologic drug arena. During the Roundtable discussions on November 21, 2008, several panel members pointed out that there are currently eight human growth hormone products on the market in the United States. The developers of all eight products were willing to conduct research and development activities on this molecule without the need to rely upon any follow-on exclusivity period. Recently, Merck & Company announced its intention to enter the follow-on biologics arena even before any statutory framework had been implemented by Congress.[4] Lilly believes that any follow-on biologics exclusivity will likely lead to the same sort of anti-competitive gamesmanship that has plagued the 180-day generic exclusivity period arising from the Hatch-Waxman Act, ultimately in some cases denying quick and certain entry of follow-on biologics at an appropriate time.

[4] *See*, Merck bets on generic biotech in strategic shift, Reuters News Service, available at http://news.yahoo.com/s/nm/20081209/bs_nm/us_merck.

Any follow-on pathway would permit the approval of biologics based upon the minimum testing of follow-on products necessary to assure that only safe and effective (safe, pure and potent) alternatives to the original biologic would be approved to market or be approved as interchangeable with the original biologic. Under any new pathway, each follow-on applicant would be required to conduct all the necessary testing to establish approvability or interchangeability.

If follow-on applicants completing the testing needed to gain approval (or to gain recognition as interchangeable) faced the prospect that, once ready to commence marketing, an additional one- or two-year delay would be imposed by the FDA before they could do so, the delay itself would operate as a significant economic disincentive to investing in the creation and testing of the follow-on product. Even worse, if during this one- or two-year period, another follow-on applicant would enjoy exclusivity in the follow-on market, the economic disincentive for other follow-on products to move forward to create and develop competing follow-on products would be even greater. The one- or two-year monopoly period for the follow-on market would entrench the position of the exclusivity holder. It would likely diminish—perhaps even eliminate—the number of potential competitors that otherwise might have undertaken the work needed to enter the follow-on market. Indeed, once it became known that a follow-on product in development had secured (or appeared likely to secure) the right to a monopoly position in the follow-on market once approved, the effect on potential competitors could be devastating.

The economic justification for creating the follow-on pathway is that the lowered market entry barriers would themselves encourage the use of the pathway by eliminating all but the necessary testing needed to establish approvability or interchangeability. The contours of the pathway itself are the incentive to use the pathway. The pathway will create an incentive to get to market first because the first marketer of an approved follow-on product or product recognized as being interchangeable gains *de facto* exclusivity and then *de facto* oligopoly as later-comers eventually get to market. In contrast, the *de jure* exclusivity of a statutory one-year or two-year prohibition on the approval of any subsequent follow-on product (or recognition of any subsequent follow-on product as interchangeable) turns this inherent incentive on its head.

A follow-on exclusivity period is also the wrong policy choice to respond to the concern that some incentive is needed to spur the development of a follow-on product or the testing needed to establish interchangeability. As noted above, if in the absence of any follow-on exclusivity provision a cadre of follow-on competitors would otherwise have had a sufficient incentive to undertake the testing required under the follow-on pathway, then the exclusivity could only have negative consequences--it would both delay the possibility of competition among follow-on products and would diminish the competition because it would at best result in potentially fewer such competing products eventually getting to market.

However, if in the absence of the exclusivity provision not a single applicant would be able to justify the needed investment in the creation and development of a follow-on product (or the testing needed to establish interchangeability), the contemplated exclusivity would not provide

a meaningful incentive to do so. In such a case, the applicant would already have the assurance of *de facto* exclusivity and *de jure* exclusivity would add nothing to the economic calculus.

The exclusivity incentive is simply superfluous in the situation where it is supposedly justified—where there will be an insufficient economic incentive for either a single applicant, much less multiple applicants, to proceed with follow-on development efforts.

Conclusion

Lilly appreciates the opportunity provided to speak at the November 21, 2008, roundtable and to provide these written comments. Finally, I would like to conclude by clarifying a comment made in response to a question raised by FTC staff concerning the appropriate length of the data exclusivity period. Lilly is not simply in favor of the longest possible data exclusivity period achievable in legislation. We are not aware of any biopharmaceutical firm calling for the maintenance of the essentially infinite data exclusivity period provided under current law. We seek only a reasonable and fair data exclusivity period of at least the 14-year patent term period originally available under the Hatch-Waxman Act. We strongly believe that the predictability of such a reasonable data exclusivity term would have the benefit of addressing the issue of patent life uncertainty inherent in the FDA approval process and patent litigation. We believe it is in the interest of the public health and consumers if the law contains incentives, such as sufficient data exclusivity, that will encourage our industry and academia to create the best medicines, not just the medicines with the best patent estates. If there are any questions about Lilly's comments, please feel free to contact me.

Sincerely,

Douglas Norman
Vice President and General Patent Counsel
Eli Lilly and Company