

Eli Lilly & Company

Friday, January 30, 2009

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Directorate-General for Competition
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Ref: 39514 - Public Consultation, Commission Sector Inquiry into Pharmaceuticals

Dear Sir or Madam,

Please find attached the submission of Eli Lilly & Company to the Public Consultation on the current Sector Inquiry into Pharmaceuticals conducted by the Commission.

Eli Lilly & Company ("Lilly") welcomes the opportunity to submit these comments on DG Competition's Preliminary Report of 28 November 2008 on its inquiry into the pharmaceutical sector. At the outset, Lilly would note it endorses the observations submitted by EFPIA on the Preliminary Report. In this submission, we will highlight certain points that are of concern to us, particularly in light of our own experience, and offer suggestions for improvements to the regulatory and patent systems.

To the extent that DG Competition would like to discuss any of the points raised in this submission, we would welcome the opportunity to do so.

On behalf of Eli Lilly and Company,

Sincerely yours,



Andras C. Fehervary
Director, Policy & Public Affairs - Europe

Cc:

Ms. Florence Bayard
Mr. Steve Caltrider
Ms. Christine S. Fields
Mr. Ian Hiscock
Mr. David Hull
Ms. Erin Huntington
Ms. Macharri Vorndran-Jones

30 January 2009

**COMMENTS ON DG COMPETITION'S
PRELIMINARY REPORT ON THE
PHARMACEUTICAL SECTOR INQUIRY**

Eli Lilly & Company (“Lilly”) welcomes the opportunity to submit these comments on DG Competition’s Preliminary Report of 28 November 2008 on its inquiry into the pharmaceutical sector. At the outset, Lilly would note it endorses the observations submitted by EFPIA on the Preliminary Report. In this submission, we will highlight certain points that are of concern to us, particularly in light of our own experience, and offer suggestions for improvements to the regulatory and patent systems. To the extent that DG Competition would like to discuss any of the points raised in this submission, we would welcome the opportunity to do so.

As discussed in more detail below, we are particularly concerned that the Preliminary Report focuses on practices engaged in by innovative pharmaceutical companies that allegedly delay the entry of generics *prior* to patent expiry while it does not devote sufficient attention to the causes of delayed generic entry *after* patent expiry. The various strategies that the Preliminary Report criticizes as comprising a “tool-box” of instruments designed to delay generic entry are, in fact, normal and legitimate practices. Many of these practices are aimed at ensuring that innovators are able to enjoy their patent rights and the period of data exclusivity protection for clinical trial data and, thus, secure a revenue stream that will fund the necessary investment in future medicine. Denying innovators the benefit of the full period of patent protection and data exclusivity would be catastrophic to the pharmaceutical sector, to the discovery and development of new innovative medicines, and, ultimately, to patients, who depend on innovators to develop tomorrow’s cures.

I. The Preliminary Report Suffers From Notable Omissions

As detailed in the EFPIA submission, analysis of competition and the impact on healthcare budgets is impossible without considering the impact of state regulation or the inflated prices paid for generic medicines. The limited analysis of state regulation in the Preliminary Report is a significant analytical defect. State regulation is central both to the Preliminary Report’s consideration of generic entry, where state controls, not innovator conduct, are responsible for significant delays, and the decline in innovative productivity. According to one report:

“More extensive prescribing and use of relatively less expensive generics in the United States has fostered a competitive generics market there, and has helped to free up financial resources that are used in turn to fund greater consumption of innovative drugs by patients for whom those medicines constitute the most appropriate and beneficial treatment option. By artificially constraining prices of innovative medicines while failing to stimulate a robust and competitive market for generic medicines, [some] European governments are missing the opportunity to create “headroom for innovation.”¹

¹ Fabio Pammoli and Massimo Riccaboni, *Innovation & Industrial Leadership: Lessons from Pharmaceuticals* (Washington: Johns Hopkins Center for Transnational Relations, 2007), p. 161

As noted in the EFPIA submission, most compellingly, the Dutch health insurers' success in achieving 80% savings by challenging pharmacists' incentives, driven by high margin retentions, to maintain high prices in tacit agreement with generics suppliers, suggests that detailed examination of the generic supply chain would yield substantial savings for Member States.² It can immediately be seen that the 5% or €3 billion alleged savings possible as a result of quicker access to generic medicines is a fraction of the savings available from more efficient generic-v.-generic competition. Further, the Dutch authorities' savings of up to €400 million in one Member State, in one year over 33 medicines far exceed the €375 million per year (€3 billion over 8 years) covering 75 products in 17 Member States, which the Preliminary Report suggests could be saved by quicker generic entry. Put another way, the Dutch *per capita* savings of €24 is many times higher than the €0.90 *per capita* saving posited by the Preliminary Report.³ These simple economics confirm the Dutch health insurer's view that generic overpayment, not alleged innovator conduct, is "the largest part of the problem."

Several further examples of the consequences of state regulation on innovation, market efficiency and consumer welfare bear mention. Both price differentiation and dynamic competition is lower in Europe than in the United States both at the product and the firm levels. Pammoli demonstrates how price convergence in Europe has been driven during the decade 1994-2004 by state intervention,⁴ adding that government intervention into the market creates markets that are more static (less competitive) and consumer welfare decreases since a higher share of the healthcare expenditures is allocated to older and/or less innovative drugs.⁵ Secondly, measures implemented by European governments focusing both on limiting demand and regulating prices have created a bias towards static – as opposed to dynamic – efficiency, with implied impact on innovation.⁶

Finally, Lilly strongly encourages DG Competition, as well as other Commission Services, to include within the scope of the Sector Inquiry a full analysis of competitiveness, resource allocation, and efficiencies in the post-patent expiry period. It should calculate the full costs to European consumers of inefficiencies in the generic segment including causes and consequences of unrealistically high generic prices and distribution margins. To achieve the end of encouraging greater efficiency and thus cost savings, Lilly supports the recommendations made by Charles River Associates in their April 2007 report, namely Recommendation 6.1 (Encouraging efficient distribution; Improve mechanisms to pass on cost savings) and Recommendation 6.2 (Encouraging an efficient off-patent market; encourage price competition in the off-patent market) as well as other measures that would lead to robust competition as quickly as possible after the relevant patents have expired.⁷

II. The Preliminary Report's Criticisms of Secondary Product Patents Are Unfounded

A. Patents Covering Incremental Innovation Must Meet the Same Standards as Patents Covering the Original Product

² Preliminary Report, p. 124.

³ Representing savings of €3 billion over eight years divided between the 415 million population of the 17 Member States in question (Eurostat population data, 19 December 2008.)

⁴ Through measures such as price ceilings, restriction of patent protection, and other measures.

⁵ Pammoli et al, *supra* note 1, p. 163.

⁶ It should be noted that some governments are implementing measures to foster competition in the off-patent market. Lilly is supportive of creating full competitiveness in the off-patent sector, with appropriate IP safeguards for patented medicines (no 'jumbo' therapeutic reference groups, etc.).

⁷ *The role of competition in encouraging efficient distribution and use of generic products* (London: CRA International, April 2007)

The Preliminary Report makes a fundamental error in suggesting that, in obtaining so-called “secondary patents” on incremental innovation, a research-based pharmaceutical company is engaged in an orchestrated plan to delay generic entry. The Preliminary Report acknowledges that incremental innovation can be of “significant importance,”⁸ yet proceeds to label a patent strategy designed to protect such innovation as one of the infamous “tools” used by innovators to deliberately delay the entry of generics. Thus, the Preliminary Report implies that it is inappropriate for innovators to file for patents protecting such innovation. In doing so, the Preliminary Report ultimately fails to recognize the importance of such innovation to new advances in medicines and to competition in the pharmaceutical sector.

The Preliminary Report’s discussion of secondary patents covering incremental innovation is based on the false premise that such secondary patents are of lesser quality than the primary patents covering the original product. The terms “primary” and “secondary” have nothing to do with the quality of the patent. Indeed, as a matter of patent law, there is no such thing as a “primary” or a “secondary” patent. The terms are industry jargon commonly used in distinguishing between the patent covering the chemical compound (the active ingredient) and patents covering other innovation relating to that product. The distinction is a purely practical one regarding the effective exclusivity afforded by the granted patent. As we will explain in more detail below, if the patent cannot be designed around, then it might be described as “primary.” In contrast, if the patent is not a complete bar to generic market entry, but perhaps protects only a specific aspect of the innovator’s product, then it might be described as “secondary.” This distinction, however, has no basis in law and is not one applied by patent offices or national courts. Inventions, whether “break-through” developments or incremental developments (as many inventions in any industry are), are governed by the identical patent laws. Each must meet the same strict requirements of patentability over the art, i.e. it must be novel (the invention must be new) and must possess an inventive step (the invention must provide a non-obvious solution to a defined problem).

The examination of patents before the European Patent Office (“EPO”) and the opposition period ensure that patents are only issued for inventions meeting these requirements. Indeed, many patent applications never issue as patents. While imperfect, the European patent system is remarkably effective. It is recognized worldwide for its rigor and thoroughness in searching and in examination.⁹ Only about 5% of the patents granted by the EPO were opposed in 2007, and over 60% of the patents opposed were maintained as granted or maintained in an amended form.¹⁰ Thus, a mere 2% of patents that are allowed are subsequently withdrawn as a result of opposition, and a very small fraction of patents that are examined and issued are struck down upon further review in court.

It is simply inappropriate for the Preliminary Report to suggest expressly or by implication that innovation covered by secondary patents is inappropriately patented by innovators. If the invention meets the standards of patentability, then the invention is entitled to patent protection for the full patent term, whether it is a bold advance in science or an incremental improvement, and whether it is considered “primary” or “secondary” in its protection of a pharmaceutical product. It is worth emphasizing that so-called “incremental” innovation may involve radical new innovation directed to “cutting edge” formulation methods, processes, and other discoveries requiring significant research, develop-

⁸ Preliminary Report, para. 392.

⁹ Stuart Graham, *Post-Issue Patent “Quality Control”: A Comparative Study of US Patent Re-examinations and European Patent Oppositions*, National Bureau of Economic Research Working Paper Series, No. 8807, February 2002.

¹⁰ EPO Annual Report, 2007.

ment, and perhaps even clinical trial studies, to reach the claimed outcome that is referred to as "incremental innovation".

Finally, the Preliminary Report fails to recognize two fundamental principles in relation to secondary patents. First, a secondary patent cannot extend the patent term of an earlier invention because, if the second patent claims subject matter described and claimed in the first patent, then it does not meet the novelty requirement. Thus, if a compound and an original formulation of a product are fully disclosed in the compound or so-called "primary" patent, a secondary patent cannot reclaim the same compound and the original formulation. Thus, when the compound and the original formulation go off patent, generic versions of the original formulation may be placed on the market. Second, secondary patents – like all patents – can be designed around. Indeed, it is Lilly's experience that secondary patents are designed around by both innovators and their generic competitors. The incentive to design around a patent leads to more innovation and, ultimately, more competition in the sector.

B. Lilly's Secondary Patents Cover Incremental Innovation That Has Met Important Patient Needs

In its responses to the various requests for information issued by DG Competition during the course of the Sector Inquiry, Lilly has described its secondary patents. These patents illustrate the important role of incremental innovation. They also illustrate that the criticism in the Preliminary Report that secondary patents are "tools" and somehow improper is simply unfounded. These patents enabled Lilly to meet important patient needs with respect to the delivery of its products. These improvements are summarized below. Notably, these patents also illustrate the limitations of so-called "secondary" patents. As these secondary patents do not cover the original product, they do not block generic competitors from launching generic versions of the original product once it goes off patent and often are designed-around for competition on the new formulation. These secondary patents simply protect valuable incremental innovation, thus preserving the incentives for companies to continue to search for ways to improve their products.

Perhaps most importantly, secondary patents such as those described below demonstrate the important role of on-going investment and incremental innovation to meet the needs of the patient. The patent and competition laws should encourage such investment and the competition that results. As such the sweeping statements of the Preliminary Report disparaging such patents as merely being tools in a toolbox improperly used is simply unsupported and unfounded. Any abuses (and Lilly does not accept that the Report establishes any abuses) are the exception not the norm.

Prozac® Oral Solution and Dispersible Tablets. Lilly developed a fluoxetine (Prozac®) oral solution and a fluoxetine dispersible tablet (i.e. a tablet that is dissolved in a glass of water prior to administration). Both formulations addressed an identified patient need – product formulations that are easier for patients to swallow. Both the oral solution and the dispersible tablet formulations provide a more convenient means of administration, particularly for patients who have difficulty in swallowing tablets or who are unwilling to have tablets administered to them. The Prozac® oral solution was launched in January 1993 (United Kingdom), September 1993 (Denmark), and October 1996 (France). Prozac® dispersible tablets were launched in May 1996 (Denmark) and February 2001 (France). The patents to the solution formulation were claimed in the original fluoxetine patent filed on 9 January 1975. The patents to the dispersible tablet was filed on 20 July 1994. The expiry of exclusivity for the original product is January 2000 (United Kingdom), January 1996 (Denmark), and January 2002 (France). When the patent on fluoxetine and the original capsule formulation expired, generic companies quickly launched fluoxetine capsules without fear of infringement of Lilly's patent on the dispersible tablet formulation. Thus, patients and their physicians could choose between the

convenience provided by the proprietary dispersible tablet formulation and the generic capsule formulations. Moreover, generic companies remained free to design around the patented dispersible tablet formulations, which is what happened in practice. Non-infringing generic dispersible fluoxetine products were placed on the market and coexist on the market with Lilly's dispersible Prozac® product and fluoxetine capsule products.

Prozac® Weekly Dosage. Lilly invested in the discovery and development of a once-weekly formulation for Prozac®, which offered patients greater convenience than the original daily formulation. The patent directed to this formulation was filed on 29 May 1996. Since the patent on this new formulation only covered the new, once-weekly formulation, when the patent on the original daily formulation expired, generic companies quickly launched the daily formulation. Thus, patients and their physicians could choose between the convenience provided by the proprietary once-weekly formulation and the original (but now generic) daily formulation. Moreover, generic companies remained free to design around the patented weekly-dosage formulation.

Zyprexa® Velotab® Orodispersible Tablet. Lilly developed the Zyprexa® Velotab Orodispersible Tablet for patients who are unable or unwilling to take the original tablet. The dispersible form represents a substantial benefit for patients and health care professionals because, once the dispersible tablet is in contact with saliva, it will dissolve almost instantly in the patient's mouth, so the patient is not able to spit it out. This issue of ensuring that the patient takes the drug is particularly relevant with the psychotic patients treated with Zyprexa because they are often agitated and/or try not to take the drugs without the health care professional's knowledge. The Zyprexa® Velotab Orodispersible Tablet was launched in January 2000 (Denmark and the United Kingdom) and January 2002 (France). The patent expiry for the original tablet form is September 2011. The patent directed to the orodispersible tablet was filed on 23 September 1996 and expires in 2016. This patent will not provide exclusivity to the original tablet form beyond September 2011.¹¹

III. Enforcement of Patents Prior to Expiry Is Proper and in Accordance with Competition Law

Contrary to what is suggested in the Preliminary Report, an innovative pharmaceutical company's enforcement of its patent rights prior to expiry is neither improper nor anti-competitive. In this regard, it is critical to distinguish between the two phases in the life cycle of a pharmaceutical product: pre- and post-patent expiry. In the first phase, Lilly, like other innovators, invests massive resources into the discovery and development of innovative medicines directed to unmet medical needs. Lilly invests in both early research and development to identify innovative therapies and clinical trials that are often massive in magnitude, to assess the safety and effectiveness of new therapies in patents. In 2007, Lilly invested almost US \$3.5 billion in research and development – equivalent to nearly 19% as a percent of net sales.¹² This investment holds the hope – but not the promise – of new treatments for patients. This investment is recouped during the period of exclusivity provided by patents and any applicable data package exclusivity. In the second phase, the product is not protected by a patent or any applicable data package, and generic competition will and should quickly enter the market. The date of expiry of the exclusivity is properly the trigger point for this competition. Throughout the period of exclusivity, the pharmaceutical life cycle continues with the discovery and introduc-

¹¹ The patent on the compound remains in force in the EU 27; however, in markets not having compound protection, generic companies have designed around the orodispersible formulation patent..

¹² Eli Lilly and Company's 2007 Annual Report

tion of new, innovative products. It is only possible to bring these new and innovative products to the market through the reinvestment of profits obtained during the period of patent and data exclusivity.

Under the patent laws, patent owners have a right to enforce their patent rights and to obtain all available relief for infringements, including damages and injunctive relief. Indeed, a patent owner's enforcement of its patent rights simply reflects the fundamental right of access to justice that may not be curtailed except in the rare case of sham or vexatious litigation. Moreover, the enforcement of these rights is essential to investment and innovation in the industry. If a patent holder is ultimately proven wrong in doing so, existing measures such as the award of costs and the surrendering of any bond in place for an injunction are adequate to ensure the enforcement of this right is not abused.

IV. An Unidentified Root Cause: Generics Are Increasingly Willing to Launch "At Risk"

The Preliminary Report quite properly notes the alarming trend towards an increase in expensive and resource-consuming litigation as a product approaches the critical date of patent expiry. However, the root cause of such litigation is not the misuse of any "tool" in the "toolbox" of innovative pharmaceutical companies. Rather it is the result of a phenomenon that has not been properly analyzed in the Preliminary Report: attempts by generics to gain a first-mover advantage by obtaining early entry in the market prior to patent expiry. This attempt at early entry is commonly referred to as "at risk" generic entry because the generic company enters the market despite the risk that it will be sued by the innovator and eventually be found to have infringed the patent and have to pay damages. Such "at risk" entry triggers and necessitates patent litigation by the innovator to protect its exclusivity. Needless to say, if the patent holder could be assured that the generic entered the market even one day after the patent expired, it would not trigger litigation.

Such "at risk" entry by a generic company is nothing more than a strategy aimed at exploiting a glaring weakness in the judicial system. If the generic company had legitimate grounds to challenge the patent, it would presumably have done so early in the opposition period or well in advance of patent expiry in order to "clear the way" for the launch of the generic product. In contrast, "at risk" entry simply reflects a cynical calculus on the part of the generic company that the potential benefits of an early launch outweigh the threat of a lawsuit, regardless of the merits of any claims that it has for invalidating the patent. The generic company is simply exploiting the fact that the innovator may not be able to get timely injunctive relief because courts are either reticent to grant such relief in the first place given the complexity of patent litigation or, even if they are willing to grant such relief, they are too over-burdened or the procedure too cumbersome to allow them to do so in a timely manner. And once one generic competitor launches "at risk," others will often follow so as not to fall too far behind in market share, often making the cost and effort involved in enforcing a patent against such a host of generic companies uneconomical and impractical.

Such "at risk" launches of generics prior to patent expiry can cause irreparable harm to innovators. In some Member States, courts will not award damages that compensate the innovator for its lost profits. In cases where there are multiple generics on the market, courts may not be able to determine which generic caused the damage. Moreover, entry by generics may cause reimbursed prices to fall in a way that cannot be reversed even if the innovator eventually wins in court. Premature generic entry in one Member State may also affect price and reimbursement in other Member States, even when there is still patent protection and no generic entry in those other countries. Ultimately, the early pre-patent expiry launch of generics is highly anti-competitive because it disrupts the pharmaceutical product life cycle and may chill the introduction of new medicines essential to medical advances and lasting competition in the industry.

In addition to the irreparable harm to the innovator, early “at risk” launch of generics generates unnecessary litigation that strains the regulatory and judicial systems. Generic companies push for earlier and earlier launch so as not to be a late market entrant. Innovators respond by rushing to courts or other agencies to protect their patent rights by requesting urgent and preliminary remedies.

IV. Proposals for Reform

A. Greater Transparency and An Opportunity to Clear or Confirm Patent Rights

The problem posed by the increasing trend of expensive patent litigation (and any alleged anticompetitive behaviors associated with it) would be solved if laws and regulations required greater transparency and gave innovators an opportunity to confirm their patent rights where generic companies did not choose to “clear the way.” A generic company is presently afforded at least two opportunities to clear the way: it may oppose the patent at the time of grant or it may seek to revoke the patent subsequently in the national courts at any time. In sharp contrast, the innovator may only learn of potential infringement and initiate patent enforcement proceedings post-approval or later when the generic launches “at risk.”¹³

Many of the problems identified on the Preliminary Report and arising out of the “at risk” launch of generics prior to patent expiry could be addressed by giving the innovator an opportunity to confirm its patent before the launch of the generic. One possible approach would be to require the generic company to notify the innovator when it files an application for a marketing authorization. Such a notification would not delay the grant of the generic marketing authorization (and could be wholly independent of the health regulations for the dossier), but it would give the innovator advance warning of the launch of a generic and allow it to confirm its patent rights in court before the generic product is approved and placed on the market. Of course, if the generic company is willing to provide assurance that the generic product will not be launched until after patent expiry or, in the case of “secondary” patent protection, adequate evidence is provided to demonstrate that the generic product will not infringe the innovator’s patents, then litigation before the courts can be avoided without legal dispute.

This notice coupled with right to bring judicial proceedings (which only requires an acknowledgement of standing) sufficiently in advance of product launch to confirm its rights for an infringing product, would transform the competitive landscape in a way that ensures on-going innovation and would eliminate any improper delay of generic entry due to intellectual property rights.¹⁴ If the patent is confirmed as valid, the generic company is properly put on notice that it must wait until expiry or it must design around any patents. If the patent is held to be invalid, the way is cleared for launch upon approval. Such transparency provides significant certainty and predictability, which will reduce the risks for generics and innovators, greatly reduces the amount of patent litigation, and will foster greater competition during the patent period and post-expiry.

Such a prior notification system would not constitute “patent linkage,” i.e. it would not prevent generics from approval or launching their product on the market. The national health authorities

¹³ The point at which the innovator has standing to enforce its patent varies from Member State to Member State and is generally at pricing review or even at the point of “at risk” launch.

¹⁴ The notice would presumably trigger an exchange of correspondence between the generic and innovator with undertakings by both sides regarding the patent, design around, intent to launch, etc. Only if these undertakings do not resolve questions would matters escalate to patent litigation.

would remain free to process the generic dossier without regard to patents or the status of any litigation. They can continue to carry out the critical task of determining whether the generic product is safe, effective, and equivalent to the branded product. Any notification and clear-or-confirm measures could operate wholly outside of this approval process. It could be accomplished by simply requiring notification and granting standing in the national courts for the patent owner to bring an action in sufficient time to reach a decision prior to launch. Even without a common patent court, it will substantially decrease patent litigation. With an “at risk” generic launch, the innovator is left with no choice but to bring an action in every Member State against every generic version of its product. In a notification/confirm-or-clear system, it is likely that the first generic product will be litigated fully in one or maybe two Member States. If the patent is affirmed or falls, the leading case will likely dictate matters for other cases. All parties as well as the judicial system will benefit from a huge savings in resources.

B. European Patent Court

The greater transparency resulting from a system of a clear-or-confirm system could be coupled with the creation of a central patent court. As the Preliminary Report notes, the creation of such a court would eliminate instances where the same EPO-issued patent is litigated in multiple Member States. Lilly supports the creation of a competent central patent court provided that it is governed by rules of procedure that enable a thorough and just resolution of the issues, including rules providing limited disclosure requirements and provide for cross-examination of evidence (including expert evidence) to evaluate the veracity of evidence. However, Lilly believes that many of the problems that a central patent court would address could be eliminated by the adoption of a clear-or-confirm system that encouraged generic companies to clear the way or the branded companies to confirm their rights well in advance of the launch of a generic product. Once the way is confirmed or cleared in one or more Member States, it is unlikely the generic competitor or the innovator will continue to litigate the patent in each Member State. While there is some divergence among national courts in the application of the patent laws, there is also considerable consistency as courts recognize that a common interpretation of the laws should be achieved whenever possible. As a result, such redundant litigation becomes unproductive for all parties.