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PHARMABULLETIN Issue 3, Fall 2005

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PHARMABULLETIN Issue 3, Fall 2005

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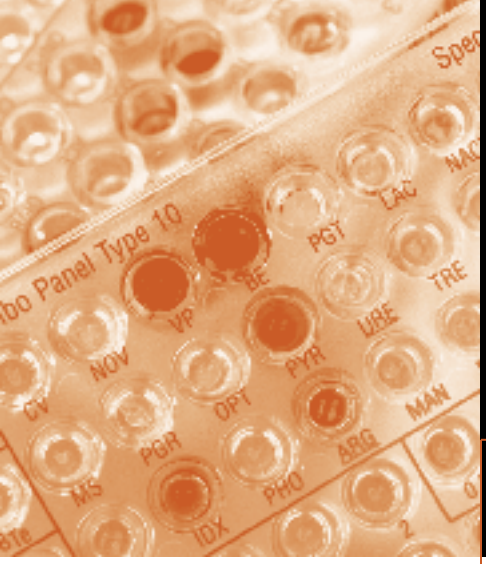
Abstract

On August 15, 2005, the Food and Drug Administration (FDA) and the Association of American Medical Colleges released a joint report that examines possible steps to accelerate drug discovery and development. The report, entitled Drug Development Science: Obstacles and Opportunities for Collaboration Among Academia, Industry and Government, is the product of a two-day conference among leaders from the pharmaceutical industry, academia, and FDA. The goal of the conference and the report was to explore means of overcoming the high failure rate for tentative drug candidates.



WILMER CUTLER PICKERING
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PHARMABULLETIN

REGULATORY

UNITED STATES

A High-Level Report on Accelerating Drug Discovery and Development in the United States

On August 15, 2005, the Food and Drug Administration (FDA) and the Association of American Medical Colleges released a joint report that examines possible steps to accelerate drug discovery and development. The report, entitled *Drug Development Science: Obstacles and Opportunities for Collaboration Among Academia, Industry and Government*, is the product of a two-day conference among leaders from the pharmaceutical industry, academia, and FDA. The goal of the conference and the report was to explore means of overcoming the high failure rate for tentative drug candidates.

The report explores issues relating to FDA's Critical Path initiative, including:

- The challenges in translating biomedical knowledge and the rapidly growing number of potential disease targets into validated targets for drug discovery
- The importance of identifying and validating clinical biomarkers in both animal models and humans, and of validating biomarkers as surrogate end-points; and
- The need to reduce inefficiency in late phase clinical trials by use of new techniques and approaches to improve trial design and operations

The report concluded that there are several important opportunities to accelerate drug discovery and development. Among the major recommendations are that government, academia, and the pharmaceutical industry should work together to:

- Develop collaborative mechanisms to enable sharing of toxicology data across industry and the FDA
- Establish an inventory of validated biomarkers
- Create a consortium to analyze and learn from failed clinical trials
- Identify and propose to Congress new regulatory incentive policies for small market drugs
- Establish a public-private partnership to carry out whole genome association studies and deposit the data in the public domain

In the past year, FDA has encouraged an active dialogue with industry regarding ways to enhance the drug approval process, and this report describes an important set of policy questions and possible solutions.

FDA /AAMC Joint Report

EUROPE

EU Parliament Proposes Changes to EU Draft Regulation on Compulsory Licensing of Patented Pharmaceutical Products

On July 19, 2005, the EU Parliament published a report proposing changes to the EU Commission's draft regulation on compulsory licensing. Following the WTO General Council Decision of August 30, 2003, the draft regulation provides a two-level procedure to lift EU patent protection of pharmaceuticals so that generics manufacturers can export them to developing countries. First, an eligible importing country (or, with such a country's approval, a non-governmental organization or a United Nations body) has to notify the WTO (or, in case or a non-WTO member, the EU Commission) of its intention to use the system. Second, any person (e.g., generics producers) can then apply to the competent EU Member State authorities for a compulsory patent license to manufacture and export the pharmaceutical product in question. Except in emergency situations, the application can only be made if the applicant tried unsuccessfully for 30 days to obtain a negotiated license from the patent holder. The EU Parliament proposal would allow the Commission to establish criteria determining the level of remuneration

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US Supreme Court issues opinion with potentially enormous implications for pharmaceutical research and development

for the patent holder. Overall, it reflects a more favorable approach towards compulsory licensing by widening the scope of eligible importing countries (no longer limited to WTO members) and by relaxing the application-related procedural requirements. However, the draft regulation may still be modified by other EU institutions.

EU Parliament Report

Amended German Medicines Act Enters into Force

The 14th Amendment of the German Medicines Act entered into force at the end of August 2005. This implements various EC Directives relating to human tissue quality and safety and herbal and human medicinal products, and amends the Cure Advertisement Act (HWG).

Unfortunately, the amended HWG does not provide the degree of liberalization of the drug advertisement market that had been expected. The provisions relating to the advertisement of non-prescription but prescribable drugs (for example, Antazida and H2 receptor blockers) have been expanded and the number of diseases for which drug advertisement outside expert circles (essentially, physicians and pharmacists) is forbidden has now been restricted to severe infectious diseases, malicious neoplasm, addiction diseases and illnesses connected to pregnancy and post-pregnancy. However, the permitted range of advertisement activities has not been significantly enlarged: the advertisement of ethical drugs, for example, remains excluded outside expert circles. In addition, effective as of April 1, 2006, misleading and/or suggestive advertising relating to plastic surgery is prohibited.

Medicines Act Amendment

INTELLECTUAL PROPERTY

UNITED STATES

Supreme Court Broadens Infringement Safe Harbor for Drug R&D

In June, the Supreme Court issued an opinion in *Merck v. Integra* that has potentially enormous implications for pharmaceutical research and development. By more broadly interpreting a "safe harbor" from infringement, the Court may have effectively immunized a significant portion of drug research, at the expense of owners of patents relating to drug targets, lead compounds, discovery methods and, possibly, research tools. As a result, universities, biotech companies and big pharma may all wish to reassess their US patent strategies and research activities.

The *Merck v. Integra* case centered on a statutory exemption from infringement of a "patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law" regulating drugs. The Court of Appeals for the Federal Circuit had previously held that this exemption in the Hatch-Waxman Act was narrowly tailored and permitted "premarket approval activity conducted for the sole purposes of sales after patent expiration" (*Hoechst-Roussel v. Lehman* (1997)) in order to "facilitate the immediate entry of safe, generic drugs into the marketplace upon expiration of a pioneer drug patent" (*Integra Lifesciences v. Merck* (2003).) However, the Federal Circuit ruled that it did not "encompass drug development activities far beyond those necessary" for FDA approval; "globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process;" or "reach any exploratory research that may rationally form a predicate for future FDA clinical tests". The Federal Circuit Court further warned that expansion of the exemption "to include [such] activities would effectively vitiate . . . biotechnology tool patents" and "swallow the whole benefit of . . . some categories of biotechnological inventions" (*Integra*).

However, the Supreme Court disagreed—at least in part. Reversing the decision of the Federal Circuit, it held that the exemption "extends to all uses of patented inventions that are reasonably related to the development and submission of any information" to the FDA; that this "necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process;" and that there "is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included." On the other hand, it held that "[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce" is not protected. Although the Court specifically declined to address research tool patents, it left the question open as to whether they were exempted.

While it is clear that the scope of the exemption has now been expanded—uses in preclinical investigations, uses that do not result in FDA submissions and uses unrelated to pre-expiration submissions for a generic drug may fall within it—its breadth remains unclear. Until further clarification is received from the Federal Circuit and, perhaps, the Supreme Court, owners of patents relating to drug targets, lead compounds, discovery methods and research tools may wish to reassess their US patent strategies and research activities, both in terms of the value of their patent rights and the risks of infringement.

Merck v. Integra (2005)

EUROPE

UK Ratifies Revised European Patent Convention

In July 2005, the UK became the fourteenth member state to ratify the amendments to the 1973 European Patent Convention (EPC), agreed by diplomatic conference in 2000.

The revised EPC aims to adapt 'the existing 1973 EPC to more effectively promote innovation and economic growth within Europe', integrating developments in international patent law—in particular the TRIPS Agreement and the Patent Law Treaty. It is now expected to take effect not before late 2007.

The UK ensured compliance with the amended EPC provisions with the passing of the 2004 Patent Act in July 2004. A number of the key provisions of this Act entered into force on January 1, 2005. These impact upon remedies in entitlement proceedings, compensation of employees for certain inventions, threats of infringement proceedings, costs and expenses in infringement proceedings and enforcement of damages. A further set of provisions, including those relating to co-ownership, patent office opinions and security for costs, entered into force on October 1, 2005. The remaining provisions shall enter into force when the revised EPC takes effect, ensuring greater consistency and conformity with the practice of the EPO.

2000 EPC

Patents Act 2004

UK Patent Office Issues New Patentability Assessment Practice Notice

In light of two recent judgments from the High Court, the Patent Office has issued a new Practice Notice advising of the approach its examiners shall now take to the examination of patentability.

It advises that examiners should first look at the substance of the claim as a whole and identify the new and non-obvious advance in the art. They should then determine whether this advance is in fact new and obvious (and capable of industrial application), in light of the description of "invention" as set out in Article 52 of the EPC. Finally, they should consider whether the new and non-obvious element identified falls under the category of excluded matter, as set out in the 1977 Patents Act (as amended).

While the Office considered that the new approach should be applied with "immediate" effect, it does not materially affect the boundary of what is patentable. Each application shall continue to be assessed on its merits and account shall be taken of arguments put forward by the applicant. Furthermore, this approach remains subject to additional guidance by the courts. In the meantime, the clarification it offers and the attempt to harmonize with the approach of the European Patent Office (EPO) is welcomed.

In the Matter of CFPH LLC

Halliburton Energy Services v. Smith International

Patent Office Notice

ANTITRUST/COMPETITION

UNITED STATES

FTC Asks Supreme Court to Review Legality of Patent Settlement Agreements between Branded and Generic Manufacturers

On August 29, 2005, the Federal Trade Commission (FTC) filed a petition for writ of certiorari in the Supreme Court seeking review of an Eleventh Circuit Court of Appeals Decision against the FTC. As reported in the last issue, the Eleventh Circuit had reversed an FTC cease and desist order and had upheld the legality of two agreements settling patent infringement claims between branded manufacturer Schering-Plough and generic manufacturers Upsher-Smith and ESI Lederle, respectively.

The FTC seeks review on the question whether "an agreement between a pharmaceutical patent holder and a would-be generic competitor, in which the patent holder makes a substantial payment to the challenger for the purpose of delaying the challenger's entry into the market, is an unreasonable restraint of trade." The FTC also takes issue with the Eleventh Circuit's application of the standard of review in rejecting the FTC's earlier administrative conclusions.

In its petition, the FTC argues that the Eleventh Circuit mistakenly held that settlements "within the outer, nominal bounds of patent claims are presumed lawful." The FTC urges that such a rule fails to take into account the substantial uncertainty in both the validity and reach of patents. Rather, the FTC believes that any substantial settlement payment from the patent holder to the generic manufacturer represents a "quid pro quo" for an "agreement by the generic to defer entry beyond the date that represents an otherwise reasonable litigation compromise," reflecting the risk associated with that uncertainty.

The FTC relies heavily on its view that the Hatch-Waxman Act signaled clear Congressional intent to foster generic entry and encourage challenges to blocking patents. That intent overrides, in its view, any public policy in favor of litigation settlement. It also cites empirical reports of successful generic challenges to such blocking patents, and of reduced consumer cost associated with increased use of generics.

The Supreme Court has full discretion whether to accept the matter for review. There is no set

FTC seeks review on whether an agreement between patentee and generic competitor, involving a substantial payment to delay market entry, is 'an unreasonable restraint of trade'.

timetable for that determination, but it could well occur in October or November of this year. If the petition is granted, additional briefing and argument would be considered before any ultimate decision.

FTC Petition

EUROPE

European Commission Fines AstraZeneca 60 Million Euros for Misuse of Patent System

On June 15, 2005, the European Commission fined Anglo-Swedish group AstraZeneca €60 million for abusing its dominant position by:

(1) Giving misleading information to several national patent offices within the EEA in order to obtain supplementary protection certificates, giving extended patent protection for its ulcer drug, Losec; and

(2) (After AstraZeneca switched to a tablet version of Losec) Asking national agencies to de-register market authorizations for the capsule formulation of Losec, preventing generic producers from offering rival products.

The Commission concluded that these actions, which took place between 1993 and 2000, made it almost impossible for other companies to launch competing generic products (keeping prices artificially high) and prevented parallel imports, and therefore amounted to an abuse of a dominant position.

The Commission's decision could signal a much stricter approach towards European pharmaceutical companies. While this type of conduct has in the past been found to violate US antitrust law, it is the first time the Commission has applied Article 82 EC Treaty in this way. Indeed, a Commission official confirmed that, because of the novelty of the situation, the *"fine was lower than it would otherwise have been."*

AstraZeneca has appealed the Commission's decision to the European Court of First Instance.

AstraZeneca Fined

OFT Launches a Review of NHS Procurement of Branded Pharmaceuticals

On September 13, 2005, the UK Office of Fair Trading launched a study into the Pharmaceutical Price Regulation Scheme (PPRS), the non-statutory scheme agreed between the Department of Health and industry to control the profit margins of manufacturers of branded pharmaceuticals, that have been licensed for prescribing on the NHS. The move comes only months after the PPRS was renewed until 2005. The study forms part of the OFT's examination of public procurement in the UK.

It is expected that the OFT will report on the findings of the study in Spring 2006. If the OFT concludes that the PPRS is in need of reform, it could recommend that the UK government change the PPRS, refer the PPRS to the Competition Commission for a fuller investigation, or take undertakings from pharmaceutical companies in lieu of a reference.

OFT Review

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PharmaBulletin

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