Wilmer Cutler Pickering Hale and Dorr LLP

Wilmer Cutler Pickering Hale and Dorr Antitrust Series

Year 2005 *Paper* 57

Pharma Bulletin - Spring 2005

Mark Heller* Hollie Baker† Robert Barry‡

James Burling** Suyong Kim††

*WilmerHale

†

‡

**

††

Pharma Bulletin - Spring 2005

Mark Heller, Hollie Baker, Robert Barry, James Burling, and Suyong Kim

Abstract

FDA to Create Drug Safety Board In February 2005, the Food and Drug Administration (FDA) announced that it will create a new independent Drug Safety Oversight Board (DSB) to oversee the management of drug safety issues within the Center for Drug Evaluation and Research (CDER). The FDA Commissioner will appoint individuals from the FDA and medical experts from other Health and Human Services agencies and government departments to the DSB, which also will consult with other medical experts and patient and consumer group representatives. Additionally, the FDA is proposing a new "Drug Watch" web page for emerging data and risk information, and anticipates an increased use of information sheets written for healthcare professionals and patients. Because of the potential concerns associated with disseminating emerging information prior to regulatory action, the agency has stated it will solicit public input. The FDA will issue draft guidance on procedures and criteria for identifying drugs and information for the Drug Watch web page.

WILMER CUTLER PICKERING
HALE AND DORR LLP

PHARMABULLETIN

Spring 2005

REGULATORY

UNITED STATES

FDA to Create Drug Safety Board

In February 2005, the Food and Drug Administration (FDA) announced that it will create a new independent Drug Safety Oversight Board (DSB) to oversee the management of drug safety issues within the Center for Drug Evaluation and Research (CDER). The FDA Commissioner will appoint individuals from the FDA and medical experts from other Health and Human Services agencies and government departments to the DSB, which also will consult with other medical experts and patient and consumer group representatives. Additionally, the FDA is proposing a new "Drug Watch" web page for emerging data and risk information, and anticipates an increased use of information sheets written for healthcare professionals and patients. Because of the potential concerns associated with disseminating emerging information prior to regulatory action, the agency has stated it will solicit public input. The FDA will issue draft guidance on procedures and criteria for identifying drugs and information for the Drug Watch web page.

The agency's announcement falls on the heels of earlier action also taken to address drug safety concerns. In November 2004, Acting FDA Commissioner Lester M. Crawford, D.V.M., Ph.D., announced that an Institute of Medicine committee would study the effectiveness of the US drug safety system and determine if additional steps could be taken to learn more about the side effects of drugs as they are actually used. Dr. Crawford announced a CDER pilot program to provide for a review of differing professional opinions by FDA and outside experts. The agency will also conduct workshops and advisory committee meetings to discuss drug safety and risk management issues, such as whether a safety concern alters a drug's risk to benefit balance; whether the agency should request that a sponsor conduct a study to address an issue and, if so, what type of study would be most appropriate; and whether a finding is unique to one product or reflects a drug class effect. These meetings are designed to include a broad array of participants, including experts from academia, the pharmaceutical industry and the healthcare community.

FDA Factsheet

FDA Statement

OVERHAUL OF EUROPE

Overhaul of EU Pharmaceutical Law

Nine years ago, the European Parliament stated that in order for the EU to remain competitive in the expanding European and international non-proprietary markets, measures should be introduced at the EU level permitting generic pharmaceutical companies to initiate experiments and regulatory preparations prior to patent and supplementary protection certificate expiration, although the marketing of their products should not be permitted until after this date.

As a result, by the end of November 2005, the EU pharmaceutical legislative landscape shall have witnessed significant changes. One new regulation and three new directives shall enter into force effecting approximately 200 alterations, ranging from definition and administration clarifications to substantial alterations to the approval process for generic products and follow-on biologicals (biosimilars). Alterations to the regulatory powers of the relevant authorities and a widening of the mandatory scope of the centralized procedure

Baltimore
Beijing
Berlin
Boston
Brussels
London
Munich
New York
Northern Virginia
Oxford
Waltham
Washington

wilmerhale.com

"By the end of November 2005, the EU pharmaceutical legislative landscape shall have witnessed significant changes."

shall take place, in addition to stricter pharmacovigilance and increased transparency.

These amendments shall permit the filing of abridged applications for generic medicinal products eight years after EU approval of the reference product (although marketing is restricted until after ten years—or eleven in the case of a new therapeutic indication of significant clinical benefit). The present reliance on the "essentially similar" test comparing a generic medicinal product to one previously authorized has been replaced with a codified definition of a "generic medicinal product"—one that has the same qualitative and quantitative active substance composition, the same pharmaceutical form, and is bioequivalent. Finally, the Committee for Human Medicinal Products technical guidelines must be taken into account by marketing authorization applicants.

Regulation on Medicinal Products for Human and Veterinary Use

Directive on Medicinal Products for Human Use

Directive on Veterinary Medicinal Products

Directive on Medicinal Products for Human Use (Herbal Products)

ECJ Rulings Erode Data Exclusivity

"Potentially sweeping changes to fundamental laws of the US patent system are on the horizon."

While the new EU Pharmaceutical Package outlined above clarifies the definition of a generic medicinal product for the purpose of abridged applications filed after the provisions enter into force, present applications rely on the outcome of two recent European Court of Justice (ECJ) rulings, the joint effect of which has been to further erode the reliance on regulatory data protection afforded to newly authorized medicines. In separate references concerning Eli Lilly and SmithKline Beecham, the ECJ held that "essentially similar" is satisfied respectively, by a medicinal product differing only in pharmaceutical form and one sharing the same therapeutic moiety, but differing as to the identity of its combined salt.

Approved Prescription Services v. UK Licensing Authority (Interested Party: Eli Lilly)

SmithKline Beecham v. Laegemiddelstyrelsen (Interveners: Synthon and Genthon)

INTELLECTUAL PROPERTY

UNITED STATES

Life Cycle Management and Proposed Patent Harmonization

The growth of the generic drug industry began with the enactment of the Hatch-Waxman Act in 1984. With the rise of generic competition, innovator drug companies embarked on creative patent strategies, tactical licensing arrangements and litigation intended to protect their market exclusivity of brand name drugs. All of these considerations—together with an understanding of the complex body of statutes, regulations and court decisions that control practice under the Hatch-Waxman Act—are vital in mapping a course for life cycle management of a drug product. Refinements and changes to the Hatch-Waxman Act continue to influence innovator drug companies' strategies for product life cycle management. The Medicare Prescription Drug, Improvement and Modernization Act of 2003 (Medicare Amendment) made a number of important changes to the Hatch-Waxman Act, including limiting the number of automatic 30-month stays to one and eliminating the district court decision trigger for 180-day generic marketing exclusivity. Prior to the Medicare Amendment, the FDA implemented guidelines clarifying what patents could be listed in the Orange Book.

Implementation of strategies for product life cycle management starts long before the expiration of the basic patent covering the innovator drug. But the principal strategy of maintaining patent protection through a stream of patentable product innovations faces the constant hurdle of shifting patent laws and regulations. Potentially sweeping changes to fundamental laws of the US patent system are on the horizon. The National Academies' Board on Science, Technology and Economic Policy (STEP) and the Federal Trade Commission (FTC) issued reports with recommendations on modernizing US patent law. A singularly important recommendation of STEP is to seek greater harmonization between US patent laws and those of other countries, including changing US patent law to guarantee the right to patent to the first inventor who files for a patent, and creating a window after a patent is issued for an opposition procedure that would permit the correction of any mistake made in granting the patent.

STEP Report

FTC Report

EUROPE

Patent Claim Construction Guidance from the House of Lords

The October 2004 *Kirin-Amgen v. TKT* judgment is significant for intellectual property practitioners operating in biotech and high-tech industries. Adjudicating on a European patent relating to inter-cellular production of erythropoietin, the House of Lords conducted a detailed review of the law on claim construction and confirmed that the principle of "purposive construction" was in accordance with the European Patent Convention. Their lordships continued to state that this did not, however, mean that the rigid application of certain formulations of this principle were appropriate in the biotech and high-tech fields. The critical question was what the skilled man would have understood as being intended by the language used in the claim.

Kirin-Amgen v.TKT (2004)

Interim Injunctions against Generics Refused

In two separate applications during the close of 2004, the UK High Court refused interim injunctions against generic pharmaceutical companies alleged to infringe European patents for crystalline clarithromycin and the cancer treatment paclitaxel, respectively. The first was refused on the basis of the "manifest weakness of the patent" (although the court noted that had the facts been contrary, the "big unquantifiable" loss represented by "price erosion" would have outweighed the "little unquantifiable" loss represented by the generic's "five months' advantage" in the market). The second was refused because of incomplete evidence and the absence of sufficient threat and damage to require urgent court intervention.

Abbott v. Ranbaxy (2004)

Mayne v.Teva (2004)

German Patent Act Amendment

Effective on February 28, 2005, the German Patent Act shall finally be updated to accord with the European Directive on the legal protection of biotech inventions. Of particular interest, the German legislature has decided that only inventions regarding precisely described commercial applications of human gene sequences and their corresponding protein may be patentable.

Directive on Legal Protection of Biotech Inventions

German Patent Act

Introduction of EU "Bolar" Provision

By the end of 2005, all EU Member States must have implemented the EU Pharmaceutical Regulation and Directives Package. This shall permit pre-patent-expiration development work, registration and generic approval, and non-infringing testing of patented medicines.

ANTITRUST/COMPETITION

UNITED STATES

FTC Supports Generic's Petition to Expand Availability of Declaratory Judgment Actions

The US Federal Trade Commission has filed a brief in support of the efforts of a generic drug manufacturer (Teva) to seek further review of a decision of the Court of Appeals for the Federal Circuit, which blocked its effort to market an alternative to the antidepressant drug Zoloft and sided with Zoloft's manufacturer, Pfizer. Under the Hatch-Waxman Act—a complex statute which governs the rights of manufacturers of brand and generic drugs—the first generic manufacturer to file a "Paragraph IV certification" challenging the brand drug manufacturer's patent obtains a period of 180 days of marketing "exclusivity," during which the FDA may not approve subsequent generic versions of the drug. However, the period does not begin to run until the first day of commercial marketing by the generic manufacturer or the date of a court decision finding the patent is invalid or not infringed. Thus, a "bottleneck" may be created where the generic manufacturer and the patent owner reach a settlement under which the generic manufacturer agrees to delay market entry in exchange for a license to the patent. The generic manufacturer still has the right to 180 days of exclusivity, but the period does not begin to run and subsequent generics thus cannot be approved.

In this case, Pfizer reached such a settlement with Ivax (the first generic manufacturer to challenge its patent), and Teva (the second generic manufacturer) sought to break the bottleneck by filing its own Paragraph IV certification. When Pfizer did not sue Teva, the company then sought a declaratory judgment that Pfizer's patent was invalid or not infringed. However, the lower court held that there was no "actual controversy" between the parties (which is required to bring a declaratory judgment suit) because there was no present threat that Pfizer would sue Teva for infringement. The appellate court upheld

"The critical question was what the skilled man would have understood by the language used in the claim."

the decision and Teva is now seeking rehearing and/or review before the full "en banc" court. Essentially, the FTC has sided with Teva on public policy grounds, arguing that, in this context, declaratory judgment actions should be allowed to proceed because they "could play an important role in furthering competitive pharmaceutical markets and in lowering healthcare costs." The FTC has previously supported challenges (and has brought them itself) to what it believes to be abuses of the Hatch-Waxman Act's provisions that impede competition by generic manufacturers.

FTC Brief

EUROPE

Advocate-General Opinion on Supply Restrictions That Limit Parallel Trade

In October 2004, Advocate-General Jacobs delivered an important opinion in *Syfait v. GlaxoSmithKline*. This was a reference to the European Court of Justice from the Greek Competition Commission on the issue of whether the protection of legitimate commercial interests can justify a restriction of supply by a dominant pharmaceutical company, which is designed to limit parallel trade. Advocate-General Jacobs considered that a refusal to supply does not automatically amount to an abuse of a dominant position within the meaning of Article 82 EC simply because the measure is designed to restrict parallel trade. Instead, he considered that a supply restriction that limits parallel trade can be objectively justified in the "highly specific" context of the European pharmaceutical industry as:

(1) normal competitive conditions do not exist in the European pharmaceutical market due to the high level of regulation which affects price and distribution;

(2) incentives for dominant companies to innovate and invest in R&D would be harmed if prices to wholesalers across the EU were effectively reduced to the lowest national price charged to wholesalers; and

(3) parallel trade in pharmaceuticals mainly benefits wholesalers, rather than purchasers.

The opinion of the Advocate-General is not binding on the European Court of Justice, whose final judgment is still awaited, although such opinions are upheld in a large majority of cases.

Syfait v. GlaxoSmithKline (2004)

PharmaBulletin

Contacts:

Regulatory
Mark Heller
+1 202 942 8488
mark.heller@wilmerhale.com

IP – US
Hollie Baker
+1 617 526 6110
hollie.baker@wilmerhale.com

IP – Europe
Robert Barry
+44 20 7645 2501
robert.barry@wilmerhale.com

Antitrust – US
James Burling
+1 617 526 6416
james.burling@wilmerhale.com

European Competition
Suyong Kim
+44 20 7872 1000
suyong.kim@wilmerhale.com