



PHARMABULLETIN

REGULATORY

UNITED STATES

FDA Issues Guidance Describing New Drug Safety Website for Emerging Risks

In May 2005, the Food and Drug Administration (FDA) issued draft guidance on the type of information to be posted on its new “Drug Watch” website—a site intended to identify drugs for which it is actively evaluating early safety signals. At this time, the FDA plans only to post information on drug products regulated by the Center for Drug Evaluation and Research, therefore vaccines, blood products and medical devices shall be excluded.

In its guidance, the FDA identified several factors that it plans to consider when determining what products and information to post on this site, including whether:

- New and emerging safety information could significantly affect prescribing decisions or how patients should be monitored (e.g., a new possible drug-drug interaction has been identified and needs to be considered in prescribing)
- Measures may be taken by providing information that could help to prevent or mitigate harm (e.g., limit prescribing to patients most likely to benefit from the drug, be alert for signs of serious adverse reactions)
- An unapproved (off-label) use of the drug appears to pose a significant risk to patients

The FDA indicated that it intends to remove products from the website as safety issues are resolved. The guidance also warned manufacturers about the consequences of emphasizing a competitor’s listing on the Drug Watch site or minimizing the effect of its own listing, indicating that neither the fact that a drug appears on Drug Watch nor the specific information posted about it will generally

constitute substantial evidence or clinical experience to support a comparative safety or effectiveness claim. Accordingly, comparative claims made in prescription drug promotion based on information posted on the site may be considered false or misleading marketing, as may a company’s representations made to minimize the effect of its own emerging risk information.

[FDA Guidance](#)

EUROPE

Abridged Marketing Authorization Applies to Line Extension Product with Different Dosage Schedule

In the most recent of four actions testing the boundaries of the abridged marketing authorization provisions relating to medicinal products for human use, the UK High Court has held—despite the fact that the European Court of Justice (ECJ) has not specifically previously considered the issue—where the data relied upon relates to an authorized product (itself a line extension of an earlier authorized product with a different dosage schedule) the principles set out in the three previous cases apply. As a result, the three generic applicants in the case were entitled to rely on such data, without addition, and a further reference on interpretation to the ECJ was held to be unnecessary.

Merck Sharp and Dohme had challenged the entitlement of the applicants to rely upon data relating to two authorized osteoporosis products in order to seek abridged marketing authorization for their own products. EC legislation states that abridged marketing authorization may be sought where the applicant can show that its product is “essentially similar” to one that has been authorized for 10 years (UK). The ECJ has held that data relating to products authorized for less than this period, but differing only in therapeutic indication, bioavailability or pharmaceutical form to one

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so authorized, may be relied upon, provided the test of “essential similarity” (same qualitative and quantitative composition, same pharmaceutical form, bioequivalent and no significant difference in safety or efficacy) remains satisfied.

[Merck v. Approved Prescription Services](#)

Automatic Validity of Swiss Marketing Authorizations in Liechtenstein Impacts Duration of Supplementary Protection Certificates

The ECJ has recently clarified that the automatic validity of Swiss marketing authorizations in the European Economic Area (EEA) member state of Liechtenstein—result of a mutual recognition agreement between these two countries—means that such authorizations do constitute the “first marketing authorization in the community” for the purpose of granting Supplementary Protection Certificates (SPC).

On joined references from the UK Patent Office and the Luxembourg Administrative Court, Swiss marketing authorizations were obtained several months before authorizations in an EEA member state other than Liechtenstein. The patentees argued that the SPC sought should run from the date of the later authorizations. The ECJ disagreed on the basis that this would mean that the patent and SPC holders should be able to take advantage of more than the permitted 15 years’ exclusivity from the date of first authorization.

SPC may be granted for any active ingredient(s), protected by patent and present in medicinal products that have received EEA marketing authorization. SPC confer the same rights as the patent and take effect at the end of its term for a period equal to that elapsing between the date the patent application was lodged and the date of the first EEA authorization. SPC compensate for the delay in commercialization caused by the authorization procedure. The maximum duration of an SPC is five years.

This decision may have significant impact for relevant patent holders. Many such patentees seek early authorization in Switzerland prior to placing their respective products on the EEA market some months later. By calculating extended protection from the date of this earlier authorization, these patentees may now face significant profit losses. In the case referred by the Luxembourg Court, the patentee lost protection for a period greater than two years. Patentees will now have to take care that their Swiss marketing approvals do not proceed faster than their EEA approvals.

[Novartis v. Licensing Authorities](#)

“UK Court of Appeal further develops principles of patent claim construction.”

INTELLECTUAL PROPERTY

UNITED STATES

En Banc Review Denied

The Spring 2005 issue of *PharmaBulletin* reported that the Federal Trade Commission (FTC) had filed a brief in support of the generic drug manufacturer to have the US Court of Appeals for the Federal Circuit review a panel decision en banc as to whether Teva—an ANDA applicant who had filed a paragraph IV certification—had a reasonable apprehension of suit to create jurisdiction for its declaratory judgment action. On April 4, 2004, this petition was denied (*Teva Pharmaceuticals v. Pfizer*).

This closely watched and controversial decision is important for both pharmaceutical and generic companies to consider in their strategic decisions on patent enforcement and generic competitor product launch.

Teva had filed an ANDA application, with a paragraph IV certification, seeking approval from the FDA to market its generic version of Pfizer’s Zoloft® (sertraline hydrochloride), before Pfizer’s patent expired. Under the provisions of the Hatch-Waxman Act, Pfizer had 45 days to sue Teva for patent infringement. When Pfizer did not sue, Teva brought a declaratory judgment action against Pfizer, seeking a determination that its generic product did not infringe Pfizer’s patent.

The court held that merely listing a patent in the Orange Book does not illustrate a “reasonable apprehension” of being sued, because listing is a statutory requirement, “more is required for an actual controversy than the existence of an adversely held patent.”

Judges Garja and Dyk wrote dissenting opinions on the denial. Judge Garja asserted that the panel decision allowed “the statutory procedures to be manipulated by the patent holders to the clear and foreseeable detriment of the generic drug industry.” Judge Dyk wanted the en banc rehearing granted in order to answer the question as to “whether a patent holder can delay [FDA] approval of an application for a competing generic drug by the simple expedient of refusing to sue for infringement.” These opinions portend further amendments to the Hatch-Waxman Act. In the meantime, patentees may consider not suing generic companies who have filed an ANDA with a paragraph IV certification, as an alternative strategy to Hatch-Waxman litigation.

[Teva Pharmaceuticals USA Inc. v. Pfizer Inc.](#)

[2003 Medicare Act](#)

EUROPE

UK Court of Appeal Further Develops Principles of Patent Claim Construction

Hot on the heels of the House of Lords decision in *Kirin-Amgen*, the Court of Appeal has taken the opportunity to further develop the principles of the construction of patent claims.

The claimants, Mayne Pharma Pty Ltd and Mayne Pharma Plc, initiated proceedings seeking a declaration of non-infringement relating to four patents owned by the defendant, Pharmacia Italia SpA. Pharmacia Italia counterclaimed for infringement of one of these patents, relating to an injectable ready-to-use anticancer solution not “reconstituted from a lyophilizate.” The sole issue at trial was the interpretation of claim one of that patent.

Finding for Pharmacia Italia, the Court of Appeal held, contrary to the trial court, that the patent was infringed by Mayne Pharma’s product, which had been subjected to a lyophilization process. Its reason was that a pharmaceutical manufacturer (the correct notional person skilled in the art) would see that the essence of the invention was the manufacture of a ready-to-use solution that did not involve the previously essential lyophilization stage.

In a short 10-page judgment, the court noted with approval that the case had been subjected to the streamlined procedure, going “from start to determination on appeal in less than 9 months” and offered the following practical guidance as to claim construction:

- The extent of protection (the monopoly) is determined by the terms of the claims.
- These are to be interpreted purposively—the inventor’s purpose being ascertained from the description and drawings.
- Purpose is not however “the be-all and end-all”; at “the end of the day” one is “concerned with the meaning of the language used.”
If, for example, a patentee has included an obvious “deliberate limitation” in a claim, this limitation has a meaning and cannot be disregarded. Equally, where a word or phrase with a particular contextual meaning is used, this word or phrase may not necessarily have that meaning in context.
- There is no general “doctrine of equivalents.”

[Mayne Pharma v. Pharmacia Italia](#)

INTERNATIONAL

India Adopts WTO Patent Law

Under legislation passed in late March, India will begin granting patent protection for pharmaceutical products, effectively prohibiting the domestic manufacture of low-cost generics. This is an important milestone for India, marking its compliance with its obligations under the WTO TRIPS (World Trade Organization Trade Related Intellectual Property Rights) regime.

The new law provides that Indian companies producing generics prior to January 1, 2005, will be permitted to continue to do so, but only if they apply for a manufacturing license and pay a reasonable royalty to the patentee. Product patents granted under the new regime will remain in force for 20 years, during which time the patentee will have exclusive rights over the manufacture and sale of the drug.

Branded pharmaceutical companies should welcome the passage of this bill. Foreign filing strategies will have to be reviewed to capture the new protections afforded by this change in patent law.

ANTITRUST/COMPETITION

UNITED STATES

Appellate Court Upholds Legality of Hatch-Waxman Settlements between Branded and Generic Drug Companies

On March 8, 2005, the Eleventh Circuit Court of Appeals reversed a cease and desist order of the FTC and upheld the legality of agreements between a branded drug manufacturer and two generic drug manufacturers settling patent infringement litigation under the Hatch-Waxman Act (*Schering-Plough Corp. v. FTC*). The FTC had ruled that the settlements were a per se illegal market allocation because they involved payments by the branded company to the generics in exchange for the generics’ agreement not to market their products until certain dates. The Eleventh Circuit disagreed and reversed the order, holding that patents are presumed valid; that the branded company had an absolute right under its patent to exclude the generics until patent expiration; and, therefore, that the settlements—which provided for generic entry earlier than the expiration of the patent—were within the exclusionary scope of the patent. The court also held that any anticompetitive effects of the settlements were reasonably “ancillary” to the “clear” pro-competitive efficiencies resulting from the settlement of patent infringement suits.

“India will begin granting patent protection for pharmaceutical products.”

The decision has potential far-reaching consequences, because a party aggrieved by a decision of the FTC may appeal to any court of appeals in which it does business. Thus, as a practical matter, if the decision in *Schering* stands (the FTC has filed a petition seeking an en banc review, and if unsuccessful, could seek review by the Supreme Court), it may become difficult, if not impossible, for the FTC to challenge most Hatch-Waxman settlements.

[Schering-Plough v. FTC](#)

EUROPE

Senior Executives Arrested on Suspicion of Price Fixing

Two senior executives of Goldshield Group plc were arrested on March 28, 2005, on suspicion of fixing the price of generic drugs. The arrests were made as part of an ongoing investigation by the UK Serious Fraud Office (SFO) into allegations that six drug companies fixed the prices of generic versions of common antibiotics (including the blood-thinning agent warfarin and the ulcer drug Zantac) in the late 1990s.

One of the companies under investigation, Ranbaxy (UK) Ltd, reached a £4.5 million settlement with the Department of Health on April 1, 2005.

Following the introduction of the "cartel offense" by the Enterprise Act of 2002, it is an offense to dishonestly agree to fix prices, limit or prevent supply or production, share markets, or engage in bid-rigging.

The SFO's investigation relates to alleged price fixing that took place before the introduction of the cartel offense. However, the arrests highlight the increasing willingness of the UK authorities to take action against individuals engaged in cartel activity.

European Court of Justice Declines Jurisdiction in *Syfait v. GlaxoSmithKline*

Following the report published in the Spring 2005 edition of *PharmaBulletin*, the ECJ stated, on May 31, 2005, that it does not have jurisdiction to rule on the issue referred by the Greek Competition Commission—namely, whether the protection of legitimate commercial interests can justify a restriction of supply by a dominant pharmaceutical company that is designed to limit parallel trade. The ECJ held that, because

the Greek Competition Commission is not a "court or tribunal," it is unable to refer questions for a preliminary ruling. The October 2004 Opinion of the Advocate-General therefore provides the only guidance on this issue.

[Syfait v. GlaxoSmithKline](#)

STOP THE PRESS

Wilmer Cutler Pickering Hale and Dorr is pleased to welcome Jeffrey K. Francer to the firm. Jeffrey is an associate in the FDA Department and will advise clients regarding the regulation of drugs, biological products and medical devices. Prior to joining the firm, Jeffrey served as associate chief counsel of the FDA.

We would like to give special thanks for this edition to Corinne Atton, Hollie Baker, Jeffrey Francer, Christopher Hutton, Peter Spaeth and Colleen Superko.

PharmaBulletin

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