PharmaBulletin

WILMERHALE

REGULATORY

UNITED STATES

FDA Approves Omnitrope but Cites Unique Circumstances for 505(b)(2) Approval

On May 30, 2006, the US Food and Drug Administration (FDA) announced that it had granted approval of Omnitrope, a recombinant human growth hormone (rhGH) manufactured by Sandoz, a division of Novartis. Omnitrope is the first follow-on version of a previously approved recombinant biotechnology drug to receive FDA approval.

The FDA's action comes almost three years after Sandoz filed a New Drug Application (NDA) for Omnitrope under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act. Section 505(b)(2) permits an applicant to submit an NDA that relies on information from published scientific literature or the FDA's finding of safety and effectiveness of another approved drug. In August 2004, the FDA notified Sandoz that it was unable to reach a decision on the application, and Sandoz filed suit in a US district court, alleging that the FDA violated 21 U.S.C. § 355(c)(1) that required the FDA to approve or deny an NDA within 180 days after filing. In April 2006, the court granted summary judgment for Sandoz and ordered the FDA to issue a decision on the application.

The FDA stressed that the approval of Omnitrope as a follow-on protein product did not provide an abbreviated pathway for follow-on biological products licensed under the Public Health Service Act. The FDA maintained that because human growth hormone is well characterized and well understood, it was uniquely suited for comparison to another rhGH product and, hence, for approval under section 505(b)(2). Sandoz's NDA relied on Pfizer's approved rhGH product Genotropin and on preclinical and clinical data generated by Sandoz. The FDA warned that Omnitrope's approval did not guarantee follow-on approval for more complex and/or less understood drugs under section 505(b)(2).

FDA Approval of Omnitrope

Report Criticizes FDA's Drug Safety Oversight

On April 24, 2006, the General Accountability Office (GAO) issued a report critical of the FDA's drug safety program. The GAO found that the FDA lacks clear and effective processes for making decisions about and providing management oversight of post-market safety actions. Specifically, the GAO found a lack of clarity regarding how decisions are made and organizational roles are defined, as well as insufficient oversight by management and data constraints. The GAO also found that inadequate communication between the FDA's Office of Drug Safety (ODS) and Office of New Drugs has slowed the evaluation process. It also concluded that the FDA lacks authority to require certain studies and has resource limitations for obtaining data. The GAO noted that some of the FDA's recent initiatives, such as the establishment of a Drug Safety Oversight Board, may improve the post-market safety decision making process, but it concluded that they will not address all gaps.

The GAO suggested that Congress consider expanding the FDA's authority to require drug sponsors to conduct post-market studies, such as clinical trials or observational studies, as needed, to collect additional data on drug safety concerns. It also recommended that the FDA systematically track post-market drug safety issues; revise and implement its draft policy on major post-market safety decisions; improve the dispute resolution process; and clarify the ODS's role in scientific advisory committees.

The FDA commented on the draft report by stating that the GAO's conclusions were reasonable and consistent with actions it has already begun or planned, although it did not comment on the GAO's specific recommendations. Some members of Congress have seized on the report as support

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for significant legislative reforms to the FDA's drug safety oversight. There are several such legislative proposals pending in the House of Representatives and the Senate. Other members of Congress suggested that they plan to wait for a forthcoming study by the Institute of Medicine on the US drug safety system before evaluating legislative reforms.

GAO Report

CHINA

Tighter Controls Over Prices in China on the Horizon

While China's current political leaders generally remain strongly committed to market reform, they are also determined to reduce social disparities and frictions by building a "harmonious society". High on the list of social problems in China is insufficient and unequal access to medical care. Large numbers of people lack health insurance and cannot afford to pay for care even if they do have insurance. The new Eleventh Five-Year Plan (2006–2010) calls for increased government spending, and the China Insurance Regulatory Commission has identified expanded access to health insurance as a major priority. In addition, the government has adopted policies to more tightly regulate the prices of drugs and medical devices. On May 19, 2006, eight government departments, including the powerful National Development and Reform Commission and the Ministry of Finance, issued the Opinions Concerning Further Rectification of Drug and Medical Device Market Prices (Opinions). The Opinions set eight priorities. The first and foremost is to lower drug prices, while allowing some upward adjustment in prices of medical devices and drugs in high demand. The Opinions also call for the monitoring of ex-factory prices and prices at the port of entry to minimize mark ups in the distribution chain. More stringent regulation, presumably by the SFDA, is mandated, particularly with respect to medical devices. Raising the prices for clinical services while reducing equipment purchases is also mandated.

It is unclear how these changes can be instituted in an environment of incomplete data and rising demand for medical care. Government control over distribution is rapidly decreasing as market reform continues and private distributors make gains at the expense of state-owned enterprises. Manufacturers will nevertheless face increasing pressure to hold their prices down. Foreign companies may face the greatest pressure.

INTELLECTUAL PROPERTY

UNITED STATES

US Supreme Court Grants Certiorari to Review *Teleflex* Decision

The US Supreme Court has granted certiorari to review the Federal Circuit's decision in *Teleflex, Inc. v. KSR Int'l.* (2005). The case concerns the issue of when a combination is "obvious" and reflects tension between the Federal Circuit's "motivation" test and a long line of Supreme Court cases.

The Supreme Court cases, starting in 1850, suggest the following test for obviousness:

> Given the known characteristics/functions of the elements of an invention, would ordinary artisans expect that the combination of these elements would result in what the patentee/applicant accomplished?

The Supreme Court's most recent decision, *Sakraida v. Ag Pro, Inc.* (1976), approvingly quotes the statement in *Great A. & P. Tea Co. v. Supermarket Corp.* (1950), that a "patent for a combination which only unites old elements with no change in their respective functions ...obviously withdraws what already is known into the field of its monopoly and diminishes the resources available to skillful men."

The Federal Circuit test requires the prior art to provide a motivation for making the combination. A brief filed by the Solicitor General said that the Federal Circuit "has transformed one means of establishing obviousness ...—proof that the prior art provided a teaching, suggestion or motivation for combining prior art references—into an inflexible requirement for determining obviousness" and has thus "extend[ed] patent protection to non-innovative combinations of familiar elements."

This case has the potential to significantly change the test applied by both the US Patent Office and the US courts.

Teleflex Inc v. KSR Int'l. (2005)

Sakraida v. Ag Pro Inc. (1976)

Great A & P Tea Co v. Supermarket Corp. (1950)

The Solicitor General... asked the US Supreme Court to review the Federal Circuit's decision... [concerning] when a combination is "obvious".

US Patent and Trademark Office's Proposed Rules—Are Drastic Changes Coming?

On January 6, 2006, the US Patent and Trademark Office (Patent Office) published two proposed rule packages: the first governing continuation applications; the second relating to the examination of patent claims. These proposals attempt to address a rising backlog of applications awaiting examination and to increase efficiency of examination.

The first proposal would substantially limit an applicant's ability to file for continued examination. Only a single continued examination would be allowed as a matter of right. Additional examinations would be allowed upon grant of a petition, showing that the amendment, argument or evidence could not have been submitted earlier during prosecution. This would result in a dramatic increase in appeals to the Board of Patent Appeals and Interferences. In addition, the benefit of a prior application could only be claimed in a single application, with the exception of divisional applications filed pursuant to a restriction or lack of unity requirement. Although, if the former benefit were claimed, all divisional applications would have to then be filed prior to issuance or abandonment of the original application. This is a significant change from the current practice of filing divisional applications in seriatim.

The second proposal limits initial examination to only ten "representative claims," which include all of the independent claims plus any dependent claims designated by the applicant. For additional claims to be examined, an examination support document (ESD) would be required. This would include a description of the pre-examination search; submission of an information disclosure statement; identification of where claim limitations are disclosed in the identified documents; and an explanation of how the claims are patentable over the cited documents. In practice, an ESP is not likely to be filed as it could create grounds for inequitable conduct charges in litigation.

The public was invited to comment on the proposals by May 3, 2006. Around 600 comments were received, the majority not being in favor. The Patent Office is currently considering these comments and intends to issue final rules by the end of the year or early next year.

Continued Examination Rules Notice
Claim Examination Rules Notice

EUROPE

ECJ Restricts Availability of SPCs for Medicinal Products

The European Court of Justice (ECJ) has clarified that a Supplementary Protection Certificate (SPC) for a medicinal product comprising "a combination of active ingredients" shall only be available where each of these ingredients exerts its own therapeutic effect.

In adopting a narrow interpretation of the relevant provision of Regulation (EEC) No 1768/92 (the SPC Regulation), the ECJ has declined to follow the opinion of the Advocate General, dealing a blow to innovative pharmaceutical companies.

The case concerned an SPC application filed by the Massachusetts Institute of Technology, relating to its Gliadel 7.7mg implant. Gliadel is a wafer, implanted after surgery, to treat malignant brain tumors. It comprises the known cytotoxic agent and active ingredient carmustine and a polymeric biodegradable excipient used to control its release, prolifeprosan. An SPC had been obtained in the United Kingdom and France, but was refused by the German Federal Patent Court. On appeal to the German Federal Supreme Court, a question on construction was referred to the ECJ.

Under the SPC Regulation, an SPC may be granted for a "combination of active ingredients" of a medicinal product, provided the product (its process of manufacture or particular application) is protected by a patent and a valid marketing authorization, and has not previously been the subject of an SPC in that Member State.

It is feared that this ruling may now discourage investment, particularly in new treatments, where excipients are combined with existing ingredients to overcome previous technical, efficacy or safety issues.

It is anticipated that this ruling will be decisive in the pending reference by the High Court of England and Wales, concerning an SPC application by Yissum Research

An SPC for "a combination of active ingredients" shall only be available where each of these ingredients exerts its own therapeutic effect.

and Development, for Silkis (a combination of calcitriol and excipients in an ointment base). An opinion by the Advocate General is currently awaited.

C-431/04 - Massachusetts Institute of Technology

ANTITRUST / COMPETITION

UNITED STATES

Solicitor General Opposes Supreme Court Review of *FTC/Schering-Plough* Decision

The Solicitor General concurred with the FTC that reverse payment settlements raise "important and complex" issues for antitrust law.

In previous issues, we have reported on the Federal Trade Commission's (FTC) petition to obtain Supreme Court review of an adverse 11th Circuit Decision rejecting the FTC's position on so-called "reverse payment" Hatch-Waxman patent settlements. In summary, the FTC asserts that any patent settlement including a payment from the branded drug patent holder to the generic challenger in exchange for a "delay" in generic entry should be illegal under US antitrust law. The 11th Circuit reversed an FTC ruling against Schering-Plough regarding two settlements (with Upsher-Smith and ESI Lederle) involving the potassium supplement K-Dur 20. The Solicitor General had declined to join with the FTC when it first petitioned for Supreme Court review in August 2005, but the Court thereafter itself requested the views of the United States (through the Solicitor General). The Solicitor General filed his brief in May 2006, urging that the FTC's petition be denied.

In his brief, the Solicitor General opposed review because the case did not provide a good vehicle for addressing reverse payment settlements. In the settlements in question, the 11th Circuit had determined (as did the FTC's administrative law judge in an initial finding) that the payments in question were bona fide royalty payments or otherwise justified and were not payments for delay. Thus, the factual dispute over the nature of the payment clouded the legal question presented. Moreover, the Solicitor General observed that there was no split in rulings among the Courts of Appeal that had considered the issue, and that the Supreme Court would likely have an opportunity to revisit the issue after more Circuits had taken a position.

Importantly, the Solicitor General concurred with the FTC that reverse payment settlements raise "important and complex" issues for antitrust law; and that "such settlements may pose a risk of restricting competition in ways that are not justified by a lawful patent, to the detriment of consumers." However, the Solicitor General did not agree with a categorical condemnation of such settlements as the FTC has asserted. Instead, "an appropriate legal standard should take into account the relative likelihood of success" of the parties' respective positions on the merits of the patent dispute, viewed at the time of the settlement. The Solicitor General suggested that a limited examination into the relative merits of the dispute could address this issue, and that a full trial on the merits of the patent claims would not be required.

On June 13, 2006, the FTC filed a supplemental brief taking issue with each of the Solicitor General's arguments against granting review. The Court is likely to rule on the FTC's petition by the end of June. Particularly in view of the position taken by the Solicitor General, the FTC's petition is not likely to be accepted.

IF YOU HAVE ANY QUESTIONS OR NEED ADDITIONAL INFORMATION, PLEASE CONTACT:

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