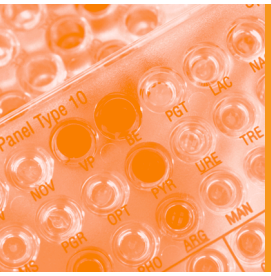

PharmaBulletin

WILMERHALE

REGULATORY

UNITED STATES

Communication Between FDA and Sponsors Makes the Drug Review Process More Efficient

The Food and Drug Administration (FDA) recently released an independent report by global strategy and consulting firm Booz Allen Hamilton (Booz Allen) analyzing the factors that affect the review of applications for drugs and biologics. The report identifies and discusses the factors that have been found to contribute to "a multi-cycle review versus a first-cycle approval." The study was mandated by the Prescription Drug User Fee Amendments of 2002.

One notable finding is the positive impact that End-of-Phase 2 (EOP2) meetings have on first-cycle approval rates. The report states that "[o]f 46 products with EOP2 meetings, 52% received first-cycle approval, vs. only 29% for products that did not have such meetings." Pre-New Drug Application/ Biologics License Application meetings were also found to be important, although not as beneficial to first-cycle approval rates as EOP2 meetings. The report points out, however, that pre-submission meetings with the FDA do not always prevent multiple review cycles. Even when major deficiencies are identified prior to submission, sponsors do not always address them. Booz Allen noted that safety and efficacy issues were the least likely to be resolved by the first review cycle, probably due to the more complicated nature of these issues.

For sponsors to reap the most benefit from pre-submission meetings with the FDA, Booz Allen found that the communications have to be effective and the timing has to be right. Problems relating to issue identification and resolution are mainly due to deficiencies in the effectiveness and timing of FDA–sponsor communications. The report therefore recommends an "open and accountable communication system centered around issue resolution," including the implementation of a checklist generated by the FDA to guide discussions and help evaluate sponsor progress. It also recommends follow-up mechanisms, such as meeting minutes and teleconferences, as well as review by the FDA of sponsor-submitted plans of action proposing approaches to issues raised. Booz Allen determined that a revised communication system is of crucial importance, especially in light of the finding that effective communication and timely responses to FDA requests for information (within one or two weeks) contribute to favorable first-cycle outcomes, whereas ineffective communications and a lack of responsiveness by sponsors lead to multiple review cycles. While the report acknowledges that the restructuring of FDA–sponsor meetings or the introduction of new meetings may have significant resource implications for the agency, it predicts that savings resulting from reduced multi-cycle reviews may "off-set increased resource demands."

Booz Allen Hamilton Report

CHINA

Corruption Crackdown in China

Chinese authorities have initiated an intensified crackdown on official corruption, with particular attention to the drug and medical devices regulatory arena. On January 12 the state procuratorate in Beijing took six officials of the State Food and Drug Administration (SFDA) into custody, including two of the most senior officials in charge of drug registration and the Secretary-General of the Chinese Pharmacopoeia Commission (CPC). This follows on the heels of the arrest of a former official of SFDA's Medical Devices Department last June.

The SFDA is responsible for the regulation of drugs and medical devices while the CPC is responsible for the formulation of

Problems relating to issue identification and resolution are mainly due to deficiencies in the effectiveness and timing of FDA–sponsor communications.

national drugs standards and the compilation of the Chinese National Pharmacopoeia. Both exercise great authority within their respective spheres of jurisdiction—a fact that, coupled with weak controls on the exercise of bureaucratic discretion, creates abundant potential for the exercise of undue influence.

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For example, the new drug registration process in China can be expected to take anywhere from two and one-half to five years under the Drug Registration Administration Measures (2005). However, as with many other regulatory bodies in China, a number of agencies have emerged with a claimed capacity to expedite approvals or registrations. Many of these agencies have connections with officials in the regulatory bodies, and are often led or staffed by former officials of such bodies. While informed agents can provide a useful and appropriate service by helping their clients to navigate a complex and often opaque regulatory process, in some instances their success is aided by the provision of illegal benefits to officials who have the ability to advance or delay applications.

Efforts to improve the regulatory process have sometimes inadvertently aggravated the temptation for corruption. Prior to the Drug Administration Law, which was enacted in 2001, provincial regulatory bodies had the power to register drugs in accordance with local standards. The law centralized such authority in the SFDA and made registration, even of existing drugs, subject to national standards. This change jeopardized the business of drug manufacturers in many localities with uncertain prospects for satisfying national standards.

The medical devices industry is also vulnerable to corruption. National or even industry standards do not exist in China for most medical devices: this allows the SFDA the latitude to accept producer or company standards for particular devices.

The drug industry was identified as one of the leading corruption targets earlier this year. Foreign manufacturers have already been subject to corrupt practices legislation in their home countries with respect to their businesses in China, as witnessed by the prosecution and subsequent fine imposed on Diagnostic Products Corporation in the United States in 2005. They, like their domestic counterparts, can now expect somewhat more vigorous efforts to combat corruption in China, as well. How effective those efforts will be remains to be seen.

INTELLECTUAL PROPERTY

UNITED STATES

Supreme Court Hears Arguments on Patentability of a Law of Nature

On March 21, 2006, the US Supreme Court heard oral argument on whether a patent for a diagnostic test for detecting vitamin B deficiency was to be construed so broadly that it would cover natural phenomena outside the scope of patentable subject matter. The question the Court specifically asked was whether a method patent that set out an indefinite, undescribed and non-enabling step directing a party simply to "correlat[e]" test results, could validly claim a monopoly over a basic scientific relationship used in medical treatment, with the effect that such patent will necessarily be infringed by any doctor simply thinking about the relationship after looking at a test result.

At issue is the patentability of many patents directed to medical diagnostic methods. Given the questions and comments from the justices and answers from litigants, most observers, however, expect that the decision may be remanded to the lower courts so that the arguments on the Court's question can be more fully developed. Further commentary on this case shall be reported in a subsequent issue of *PharmaBulletin*.

*Laboratory Corp. of America v. Metabolite Laboratories, 126 S.Ct. 601 (2005), (No. 04-607)**

Federal Court Considers Product-by-Process Claims

A recent decision by a divided US Court of Appeals for the Federal Circuit has emphasized the limited usefulness of "product-by-process" claims for product life cycle management of branded drugs. In *SmithKline v. Apotex*, the Federal Circuit held that a product-by-process claim for paroxetine, which claimed the drug was made by a new process, was anticipated based on the earlier patent for the drug and, therefore, was invalid. *SmithKline*, which markets paroxetine as Paxil®, were defending this drug against a generic challenge by Apotex.

Product-by-process claims have always been peculiar claims in US patent law. An early decision held that these claims are limited and defined by the process, but patentability was based on the product itself, not on the method of production *(Re Thorpe)*. Yet, to find infringement, there are two irreconcilable court decisions: *Scripps v. Genentech*, which held that infringement is satisfied if the accused product was made by any process; and *Atlantic v. Faytex* which held that infringement is satisfied only if the accused product was made by the same claimed process.

The Federal Court has left unresolved the question of whether the "process" portion of product-by-process claims were limitations for the purpose of infringement, expressly stating that *"[w]e take no position on whether a product-by-process claim is construed with reference to the process steps."* The Court instead focussed on the narrower issue, holding that *"a prior art disclosure of a product precludes a future claim to that same product, even if it is made by an allegedly novel process."*

SmithKline's argument that the "product" claimed was different from the prior art product fell on deaf ears; the court ruled that this argument had been waived on appeal, concluding that it was not presented in the opening brief, but buried in a footnote.

SmithKline Beecham Corp v. Apotex Corp. (2006)

*Re Thorpe, 777 F.2d 695, 698 (Fed. Cir. 1985)**

*Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991)**

*Atlantic Thermoplastics Co., Inc. v. Faytex Corp., 970 F.2d 834 (Fed. Cir. 1992)**

EUROPE

UK High Court Grants Disclosure of Litigation Experiments

In a presently unreported judgment, Pumfrey J has acceded to an Application by Debiopharm S.A. and Sanofi-Synthelabo, and held that service of a Notice of Experiments to be conducted to prove anticipation by inevitable result, waived legal professional privilege attaching to documents of "work-up" or preliminary experiments conducted prior to the drafting of that Notice.

The above parties are defendants to a claim made by Mayne Pharma Pty, to revoke four patents relating to Oxaliplatin, a treatment for colorectal cancer. Pumfrey J noted that: *"Experimental evidence is intended to provide a degree of objective confirmation or corroboration of the subjective views of the experts. It may provide, and from time to time does provide, a fixed point against which the experts may themselves be assessed...It is employed because it trumps the experts, however cogent their views may be".*

*Mayne Pharma Pty Ltd & Anr v. (1) Debiopharm SA; (2) Sanofi-Synthelabo [2006] EWHC 164 (Pat)**

First UK Patent Office Opinions Granted

The UK Patent Act 2004 introduced a new procedure whereby anyone can request the UK Patent Office (the Office) to issue an official non-binding opinion, on issues of patent validity or infringement. Since the procedure started on October 1, 2005, five opinions have been issued and one request has been withdrawn. In the first, involving the validity of a European (UK) patent relating to dispensing pens for the injection of insulin or growth hormone from a cartridge, the Office gave a detailed examination of the cited prior art and concluded that two of the claims lacked novelty and inventive step. In the second and third, both involving issues of infringement and validity of national patents, the Office only issued "conditional" and "tentative" opinions due to insufficient evidence. In the fourth, the Office found non-infringement on the documents submitted. The fifth is, as yet, unreported.

It remains to be seen what practical use such opinions will have and what weight the courts will afford them.

UK Patent Office Launches Mediation Service for IP Disputes

On April 3, 2006, the UK Patent Office launched a commercial mediation service for intellectual property disputes. Consistent with the encouragement of Alternative Dispute Resolution (ADR) following the 1998 amendment of the UK Civil Procedure Rules, the Office intends to routinely invite parties to consider mediation as an alternative to litigation. If parties agree, litigation proceedings shall then be stayed pending its outcome.

Service of Notice of Experiments in UK patent action waives legal professional privilege attaching to "work-up" or preliminary experiments.

ANTITRUST / COMPETITION

EUROPE

Nine people and five companies will be charged with conspiracy to defraud the National Health Service.

French Competition Council Rejects Complaints Made by Parallel Exporters

On December 20, 2005, the French Competition Council rejected complaints brought by several parallel exporters against decisions made in 2000–2002 by a number of pharmaceutical suppliers (including Pfizer, GK, MSD, Lilly, Sanofi and BMS) to limit the level of parallel exports of medicines from France to other countries in the European Union by either (1) ceasing to supply parallel exporters; or (2) imposing quotas on supplies to parallel exporters.

In rejecting the allegations, the Competition Council found that there was no evidence of a horizontal agreement between the suppliers and stated that a finding of parallel conduct was insufficient to establish horizontal collusion. Allegations of vertical restrictive agreements between the suppliers and wholesalers, which provided for preferential (and therefore discriminatory) treatment of wholesalers, were rejected on the basis that wholesalers are subject to significant regulatory constraints that do not apply to parallel exporters, and that this difference in the applicable legal and regulatory regimes objectively justified the differential treatment.

The Competition Council also rejected allegations that the pharmaceutical suppliers had abused positions of dominance by refusing to supply the parallel exporters. The Competition Council found that, irrespective of the relevant market definition, where the prices of a product are regulated, it is not an abuse of a dominant position to refuse to supply that product to a firm that (1) is not active on the market as regards to which prices are regulated; and (2) seeks to purchase the product at regulated prices to allow it to resell the product in other countries for a profit.

Decision No. 05-D-72

UK SFO Investigation Results in Conspiracy to Defraud Charges

On April 5, 2006, the UK Serious Fraud Office announced that nine people and five companies will be charged with conspiracy to defraud the National Health Service over drug prices and supply. This is the latest development in an ongoing investigation by the SFO into allegations that six drug companies fixed the prices of generic versions of certain drugs (specifically warfarin and penicillin-based antibiotics) in the late 1990s.

We would like to give special thanks for this issue to Corinne Atton, Hollie Baker, Robert Barry, Kristin Davenport, Christopher Hutton, Stephanie Philbin and Lester Ross.

*Please note that publicly accessible hyperlinks are not available for cases marked with an asterisk.

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