
Pharmaceutical Licensing in Product Lifecycle Management: Litigation and Settlement Under the Hatch-Waxman Act

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This is Part I of a two-part article. Part II will appear in the April 2003 issue of Licensing Journal. It will address issues arising from settlements of patent litigations brought by research-based pharmaceutical companies against generic drug manufacturers.

Prior to 1984, there was no generic drug industry. Although this statement may be somewhat of an exaggeration, it is not a gross overstatement. In 1984, 19 percent of prescriptions were filled with generic products; by 2000, the percentage had risen to 47 percent.¹ What happened?

In 1984, the Hatch-Waxman Act² (HWA) was enacted, its objective being to facilitate the development and marketing of generic copies of brand-name drugs.³ The HWA achieved this objective principally by lowering the standards for approval of such generic copies and by exempting generic drug development efforts from patent infringement.

From 1962 to 1984, a drug—generic or pioneer—could be approved only by filing a new drug application (NDA), which is required to contain extensive data proving that the drug is safe and effective. This meant that generic copies of brand-name drugs already proven to be safe and effective were required to be tested in the same way as the original drugs. Such testing, which involves clinical studies in

humans and is both costly and time-consuming, was a significant deterrent to the development and marketing of generic drugs. Indeed, it is currently estimated to cost approximately \$800 million to obtain NDA approval from the Food and Drug Administration (FDA).⁴

Since the 1984 passage of the HWA, generic copies of brand-name drugs no longer have to be tested in accordance with the standards applied to new drugs. Instead, to obtain approval to market a generic version of an approved pharmaceutical, generic drug manufacturers are now required only to submit an abbreviated new drug application (ANDA) comprising only very limited evidence showing that the generic drug is the same as and is bioequivalent⁵ to the approved drug.⁶

In addition, prior to passage of the HWA, any use of a patented drug infringed the patent.⁷ Generic drug makers, therefore, were not permitted to undertake development prior to patent expiration and, given the time required to undertake the studies required for approval, entry of generic drugs to market was delayed significantly beyond patent expiration. Specifically, the HWA provides:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.⁸

Therefore, generic drug manufacturers now can import into or manufacture generic drugs in the United States and undertake the necessary development work, including bioequivalence testing prior to patent expiration, without fear of patent infringement lawsuits.⁹

To facilitate early resolution of patent infringement actions, the HWA established a complex scheme for (1) giving notice to ANDA applicants of patents on approved drugs; (2) allowing holders of NDAs to bring a patent infringement action against ANDA applicants who certify that such patents are invalid or not infringed; and (3) providing a 30-month stay on

approval of ANDAs to allow for resolution of patent infringement actions.

Under the notice provisions, NDA holders are required to submit to the FDA information on all patents that claim the drug or a method of using the drug.¹⁰ The FDA then lists these patents in the so-called Orange Book.¹¹

When an ANDA is filed, the ANDA applicant must make one of four statutorily mandated certifications:

1. That there are no patents for the reference drug listed in the Orange Book
2. That patents are listed but have expired
3. That patents are listed but the ANDA applicant will not sell its generic drug until after the patents have expired
4. That patents are listed are invalid or will not be infringed by the making, using, offering for sale, selling, or importing of the generic drug¹²

If the ANDA applicant makes the fourth certification—commonly referred to as a “paragraph iv certification”—the ANDA applicant must give notice of such certification to the NDA holder, and the NDA holder can thereupon sue the ANDA applicant for patent infringement. If the NDA holder brings such action within 45 days of receiving such notice, approval of the ANDA is stayed for 30 months or until a court decision is reached, whichever occurs first. The 30-month period is intended to allow for resolution of the patent infringement action prior to the marketing of the generic drug.

To provide further encouragement to generic drug manufacturers, the HWA also provides that the first generic drug maker to file an ANDA for a pioneer drug will receive 180 days of marketing exclusivity vis-à-vis subsequent ANDA filers for generic versions of the same drug. The 180-day period begins on the earlier of a court decision that holds the listed patents invalid or not infringed or the first commercial sale of the generic product.¹³

Clearly, the HWA has had the intended effect of facilitating development and marketing of generic drugs. Innovator pharmaceutical companies have had to adjust to a world in which many of their products are “going generic” and many of their patents are under attack. Part of this adjustment has been the development of lifecycle management strategies whereby innovator pharmaceutical companies try to protect the market exclusivity of their products and preserve market share after generic copies become available.

Lifecycle Management Strategies

Lifecycle management strategies include developing or in-licensing product innovations, some of

which are patentable, and patent enforcement and settlement strategies, among others. These strategies have attracted the attention of antitrust enforcers and private plaintiffs. Some have withstood that attention better than others.

Product Innovations

One way to maintain patent protection is through a stream of product innovations, which are protected by patents and/or by marketing exclusivity.¹⁴ Examples of product innovations include, among others:

- *New Forms*: Pharmaceuticals often exist in various forms—for example, in different crystalline shapes (*i.e.*, polymorphs)—with different amounts of bound water (*i.e.*, hydrates), with different kinds or amounts of solvent (*i.e.*, solvates), or in different molecular shapes (*i.e.*, stereoisomers). Such forms, when newly discovered, are frequently patented. If a generic manufacturer wanted to make a generic version of an approved drug and the generic version would be in the patented form, as sometimes occurs, the generic manufacturer could be blocked by a patent on that form. The classic example of this strategy is Glaxo-Wellcome's patenting of a new polymorph of Zantac[®] ranitidine and its filing of patent infringement actions against generic manufacturers that were allegedly manufacturing generic ranitidine in the form of the patented polymorph.
- *New Formulations*: The safety or efficacy of products can sometimes be improved by switching to new formulations, for example, by using sustained-drug-release technologies to develop a once-a-day dosage form to replace an older form requiring multiple administrations per day. As in the case of new drug forms, if the new formulation is protected by patents, generic manufacturers would not be permitted to copy the improved formulation.
- *New Labeling*: In some cases, the safety or efficacy of a product can be improved by improving the labeling, that is, the instructions for use. If the new instructions are protected by patent or by marketing exclusivity, generic manufacturers cannot copy the improved labeling, and the inability to copy the improved labeling may preclude approval of the generic product. For example, Johnson & Johnson developed an improved dosing regimen for Ultram[®] tramadol. This improved labeling apparently enhances the safety and/or efficacy of the product, which is protected by marketing exclusivity. As a practical matter, this strategy is not effective unless the improved labeling is so critical that the generic version cannot be approved without it. Otherwise, the generic version can be approved with the old labeling, and physicians can prescribe products

"off-label," with the result that generics nonetheless can be substituted for the pioneer drug.

When product innovation is accomplished through in-licensing from another party, the acquisition can, in theory, be challenged as an unlawful acquisition under Section 7 of the Clayton Act or as an unlawful agreement under Section 1 of the Sherman Act. For example, Eli Lilly (Lilly) exclusively in-licensed rights to an innovation of Prozac[®] fluoxetine, a leading anti-depressant. Lilly apparently hoped to switch patients from the original product (a racemic mixture) to the innovated product (a resolved stereoisomer) prior to the entry of generic forms of the original product, thereby ensuring that many patients were being prescribed a product for which automatic state generic substitution laws would not apply. The Federal Trade Commission (FTC) initiated an investigation of this agreement but did not take action, apparently because a challenge would have involved showing that the new product had no advantages over the old, and that patients would not benefit from Lilly's bringing the product innovation to market years sooner than any other firm, which would be blocked from entry by Lilly's original patent until that patent expired.¹⁵

Ordinarily, internally generated product innovations would not be subject to antitrust scrutiny. Thus, it normally raises no antitrust issues to obtain, in addition to a "basic patent" claiming the drug as a new chemical entity, formulation or method of use patents that claim, for example, a specific form of an approved drug, such as a particular crystalline polymorph, or new uses for the drug. However, as a result of the FDA's Orange Book listing procedures and the automatic 30-month stay to which a patent owner is entitled when filing a patent infringement action under those procedures, certain conduct in connection with internal product innovations has been challenged under the antitrust laws.

Patent Enforcement and Settlement

A central piece of every lifecycle management strategy must include, for obvious reasons, the enforcement of valid patents against would-be infringers. In most cases, there would be little doubt concerning the validity and infringement of a basic patent on an approved drug—that is, a patent that claims the active ingredient as a new chemical entity. In some cases, however, the validity and infringement of ancillary patents, such as patents on product improvements, may be questionable. Thus, it is common for generic drug companies to file an ANDA to market a generic product after the basic patent has expired but before other ancillary patents have expired. In theory, if the pioneer company responds by filing an unwarranted infringement lawsuit, that act alone could be an act of monopolization. In practice, however, monopolization claims of that kind do not succeed,

because the Supreme Court requires that the infringement suit be "objectively baseless" in order to give rise to antitrust liability.¹⁶ The *settlement* of infringement suits, however, has caused a great deal of antitrust controversy.

Orange Book Listings

In most industries, obtaining improvement patents in addition to a basic patent has a simple consequence: The patentee can sue for infringement after expiration of the basic patent and during the life of the improvement patents if the alleged infringer's product practices an invention claimed in valid improvement patents. In the pharmaceutical industry, there are additional consequences. If the patent is listed in the Orange Book, a generic company cannot receive ANDA approval unless it has notified the pioneer company and given it 45 days to sue for infringement; and if such an infringement suit is filed, ANDA approval is automatically stayed for 30 months or resolution of the suit, whichever is shorter.¹⁷

If the additional patents are not listed in the Orange Book until after an ANDA for a given drug has been filed, the result can be that a generic drug manufacturer is required to file additional paragraph iv certifications after each new patent issues and is listed in the Orange Book. Each time a new paragraph iv certification is made, the pharmaceutical company can bring a new patent infringement suit within the 45-day period, thereby initiating a new 30-month stay.

According to the FTC, between 1992 and 2000, there were eight instances in which later-issuing patents were listed in the Orange Book after an ANDA had been filed. The additional delay caused by new 30-month stays in these eight cases ranged from four to 40 months.¹⁸ In two of those cases, the FTC or private plaintiffs brought antitrust cases challenging the Orange Book listing as an act of monopolization.

The remainder of this article summarizes the two civil actions, reports the FTC's views on Orange Book listing issues as expressed in a study undertaken by that agency as well as its views on recent legislative and regulatory activity, and concludes with a brief analysis of these matters.

Civil Actions

In *In re Buspirone Antitrust Litigation*,¹⁹ Bristol-Myers Squibb (BMS) initially sued the generic firms Mylan and Watson for infringement of a patent claiming a method of treating anxiety through the use of buspirone. Hours before that patent was about to expire, BMS listed in the FDA's Orange Book a second patent covering the use of a metabolite of buspirone to treat anxiety. BMS thereby obtained an additional 30-month stay of approval of Mylan's and Watson's ANDAs.

Mylan, Watson, 30 states, and several consumer organizations then sued BMS under Section 2 of the Sherman Act, charging that BMS had unlawfully maintained its monopoly by causing the FDA to list the second patent in the Orange Book and then fraudulently representing to the FDA that the second patent covered its FDA-approved drug, BuSpar, despite having disclaimed such coverage in order to secure grant of the patent for use of the metabolite. BMS moved to dismiss on the ground, *inter alia*, that its actions were immune under the *Noerr-Pennington* Doctrine,²⁰ which holds that petitioning the government, even if anticompetitive in intent and consequence, is not actionable.²¹

The FTC staff filed an *amicus* brief opposing the motion and, early in 2002, the district court denied the motion, largely adopting the FTC staff's three arguments. First, the court held that *Noerr-Pennington* was inapplicable because the FDA's actions in listing patents in the Orange Book are not truly governmental actions but instead are "nondiscretionary and do not reflect any decision as to the validity of the representation in a Orange Book listing."²² Second, the court rejected the argument that the listing was ancillary to the subsequent patent infringement suits, which clearly fall under *Noerr-Pennington*, because the suits could have been brought without an Orange Book listing. It is unclear how the court distinguished threats to litigate, which also are not a prerequisite to filing suit but nonetheless have been held covered by *Noerr-Pennington*. Third, the court found that even if *Noerr-Pennington* generally applies to Orange Book listings, this particular listing was based on a knowing misrepresentation of patent scope and thus fell outside of *Noerr-Pennington*.

In *Biovail Corporation*,²³ the FTC alleged similar conduct. According to the complaint, Biovail Corporation (Biovail) acquired an exclusive license to a patent that claimed not the formulation of Tiazac that the FDA had approved and that Biovail had been marketing, but an unapproved new formulation. Biovail sought to amend its NDA by changing its formulation so that it would fall within the patent claims. In the interim, Biovail listed the patent for the new formulation of Tiazac[®] in the Orange Book, thus forcing Andrx, the first ANDA filer for a generic version of Tiazac, to file a new paragraph iv certification and to withstand an additional 30-month stay. The FTC alleged that Biovail's acquisition of the exclusive license was unlawful under the merger laws and that its Orange Book listing and subsequent representations that the patent covered the approved form of Tiazac were unlawful under the laws prohibiting monopolization. The case was settled by Consent Order.

The FTC's Generic Drug Study

The FTC recently reported in its study (Generic Drug Study) how certain provisions of the HWA,

including the 30-month stay and Orange Book listing provisions, are affecting the generic drug industry.²⁴ The report includes a recommendation that the HWA be amended to permit only one 30-month stay per drug per ANDA. According to the report, this change "should eliminate most of the potential for improper Orange Book listings to generate unwarranted thirty month stays."²⁵

The report also stakes out a controversial position on the question of what patents are entitled to be listed in the Orange Book. Specifically, the report declares: "*The [HWA] Amendments do not grant the protection of the 30-month stay to every patent that a bioequivalent generic product may infringe.*"²⁶ In other words, the FTC's view is that even though certain new forms of an approved drug are deemed by the FDA to be the "same" as the approved drug for ANDA purposes, patents that claim such variants cannot necessarily be listed in the Orange Book. In this regard, the report specifically recites three "types" of patents that raise questions about listing: (1) metabolite patents (*i.e.*, patents that claim a chemical into which the approved drug is converted within the human body postingestion); (2) polymorph patents,²⁷ and (3) patents on chemical intermediates (*i.e.*, patents on chemical precursors that are used in the chemical synthesis of the approved drug product).²⁸

Analysis

The positions the FTC has advanced in its *amicus* brief in *Buspirone*, in its enforcement action in *Biovail*, and in its Generic Drug Study are troubling in three respects. First, rather than limiting itself in *Buspirone* to the argument that the company knew that the patent was invalid and therefore constituted "sham" petitioning, the FTC staff argued, and the court agreed, that the FDA's role in Orange Book listing is purely ministerial and that a company's submission of a patent to FDA for listing is therefore not "petitioning" at all. Thus, even when a pioneer company meets the regulatory requirements for listing, it will have no safe harbor and instead could be subject to creative allegations that some aspect of its conduct has an anticompetitive effect without an offsetting legitimate purpose. Second, the position that the FTC apparently took in *Biovail* and that was more clearly articulated in its Generic Drug Study report—that patents cannot be listed in the Orange Book unless they read on the pioneer drug—would undercut the statutory scheme if adopted. If a patent would be infringed by a generic version of a drug, the structure of the HWA is such that the pioneer company should receive notice and have an opportunity to file an infringement action; otherwise, the generic drug's ANDA could be approved before the pioneer company even learns of it—clearly not what the HWA intended. Third, a legislative ban on successive 30-month stays is a blunt instrument. Real and significant improvements to existing drugs can take

considerable time and investment to accomplish. The harder the research and development effort required, the more likely it is that patent issuance and listing will come after an ANDA has already been filed. Stripping the HWA protections in this circumstance would be counterproductive to drug innovation. Moreover, such an approach might encourage earlier and more dubious ANDA filings.

Addendum: Recent Legislative and Regulatory Activity

Both Congress and the FDA have undertaken to address some of the concerns expressed in the FTC report. Specifically, on July 31, 2002, the Senate passed S. 812, the Greater Access to Affordable Pharmaceuticals Act of 2002 (the GAAP Act), and on October 24, 2002, the FDA published proposed regulations,²⁹ both of which relate to patent listing requirements and 30-month stays. Both measures are intended to minimize perceived abuses of the 30-month stay and the Orange Book listing provisions of the HWA.³⁰

The GAAP Act and the proposed regulations both have the effect of eliminating the possibility of successive 30-month stays. The GAAP Act achieves this effect by eliminating the 30-month stay resulting from patent infringement actions based on infringements of patents listed after NDA approval.³¹ The proposed regulations simply reinterpret the HWA to provide that each ANDA can only be subjected to a single 30-month stay.³²

With respect to the patent listing requirements, both the GAAP Act and the proposed regulations make clear that patents claiming either the drug substance (*i.e.*, an active ingredient) or the drug product (*i.e.*, a formulation or composition) of an *approved or pending NDA* must be listed.³³ The proposed regulations also provide that product-by-process patents and method-of-use patents must be listed and that patents that claim metabolites, packaging, or chemical intermediates cannot be listed.³⁴

The proposed regulations provide that a different form of an approved drug substance (*i.e.*, a different polymorph³⁵ of an approved drug substance) *may* be the same active ingredient.³⁶ Under the proposed regulations, the NDA applicant or holder who submits patent information for listing in the Orange Book is required to declare that the active ingredient claimed

in the patent is the same active ingredient as the subject of the pending or approved NDA.

Under the GAAP Act, ANDA filers would be permitted to bring a civil action against NDA holders seeking an order requiring the NDA holder to amend or delete a patent listing made prior to NDA approval but not one made after NDA approval (*i.e.*, a post-NDA listed patent).³⁷

As of this writing, it appears probable that legislative activity will proceed slowly, if at all, at least as long as the FDA is progressing with its proposed regulations.³⁸ The proposed rules, however, are not without problems.

Concerning the 30-month-stay provisions, it is not at all clear that the FDA can simply reinterpret the HWA provisions that for nearly 20 years have been understood to permit multiple 30-month stays of the same ANDA under certain circumstances. In any event, whether by statute or by regulation, limiting each ANDA to a single 30-month stay ignores the realities of pharmaceutical research and development, where important innovations to approved products are often made well after NDA approval. In the section of the preamble that discusses benefits of the proposed regulations, the FDA does not take into account the potential harm to consumers that may result from eliminating this incentive to invest in post-NDA research and development.

With respect to the patent listing requirements, the proposed regulations are helpful in making clear that both drug substance and drug product patents must be listed; however, they do not address several outstanding issues, including what to do when a different form of a drug substance is the same as an approved drug substance.

Hopefully, these and many other questions will be considered after the comment period and will be adequately addressed prior to promulgation of the final regulations. Until then, it is difficult to predict what effects these changes will have on pharmaceutical lifecycle management strategies and on licensing as a tool for implementing such strategies. Clearly, the leverage in patent litigation settlement discussions between pharmaceutical companies and generic manufacturers will shift toward the generic manufacturers, because there will be somewhat less uncertainty about whether certain patents will be able to be listed and, more importantly, because generic manufacturers will no longer need to be concerned about being kept off the market by successive 30-month stays if they fail to reach a settlement agreement.

1. Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* (July 2002), at i, <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>.
2. The Drug Price Competition and Patent Term Restoration Act of 1984, Pub.L. 98-417, 98 Stat. 1585 (the HWA).
3. The second primary purpose of the HWA was to restore at least some of the patent term lost due to regulatory delays. *Glaxo v. Novopharm*, 110 F.3d 1562, 1568 (Fed. Cir.1997).
4. See Tufts Center for the Study of Drug Development, Tufts Center for the

Study of Drug Development Pega Cost of a New Prescription Medicine as \$802 Million (Nov. 30, 2001), <http://csdd.tufts.edu/newsevents/recentnews.asp?newsid6>.

5. In layman's terms, "bioequivalent" means that the active ingredient in the drug enters a patient's bloodstream and attains a concentration that is substantially the same as for the reference drug (*i.e.*, the previously approved drug).
6. 21 U.S.C. § 355(j).
7. See *Roche Prods., Inc. v. Bolar Pharm. Co., Inc.*, 733 F.2d 858 (Fed. Cir. 1984).

8. 35 U.S.C. § 271(e)(1).
9. The many questions about the extent of the exemption that 35 U.S.C. § 271(e)(1) leaves open are beyond the scope of this article. According to the Supreme Court, "[N]o interpretation that we have been able to imagine can transform Section 271(e)(1) into an elegant piece of statutory draftsmanship." *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 679 (1990).
10. 21 U.S.C. § 355(b)(1).
11. Food and Drug Administration, Approved Drug Products with Therapeutic Equivalence Evaluations (June 2002), <http://www.fda.gov/cder/ob/default.htm>.
12. 35 U.S.C. § 355(j).
13. 21 U.S.C. § 355(j)(5)(iv).
14. An active ingredient of a drug is protected from competition for a period of five years from the first approval of the drug. 21 U.S.C. § 355(j)(4)(D)(ii). A new use of a previously approved drug is, under certain circumstances, protected for a period of three years. 21 U.S.C. § 355(j)(4)(D)(iii). These protections are commonly referred to as "marketing exclusivity."
15. Sheila F. Anthony, Riddles and Lessons from the Prescription Drug Wars: Antitrust Implications of Certain Types of Agreements Involving Intellectual Property, presented to American Bar Association Antitrust and Intellectual Property Crossroads Program (June 1, 2000), <http://www.ftc.gov/speeches/anthony/sftp000601.htm>.
16. In *Professional Real Estate Investors, Inc. v. Columbia Pictures Indus., Inc.*, 508 U.S. 49, 113 S. Ct. 1920 (1993), the Supreme Court set forth a two-prong test for determining whether a litigation is a sham, including (1) first showing that the litigation is "objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits," and (2) then determining "whether the baseless suit conceals an attempt to interfere directly with the business relationships of a competitor." (quoting, *Eastern R.R. Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127, 144 (1961)).
17. The responsibility for submitting information concerning patents for listing in the Orange Book lies with the NDA holders. The FDA has taken the position that its role in listing patents in the Orange Book is merely ministerial, and, therefore, it does not confirm the appropriateness or correctness of the listing. There are several cases (not discussed in this article) in which generic manufacturers have sought, unsuccessfully, to require patents that allegedly do not meet the statutory requirements for listing to be stricken from the list. These cases include, e.g., *Mylan Pharm., Inc. v. Tommy G. Thompson*, 258 F.3d 1323 (Fed. Cir. 2001).
18. Federal Trade Commission, Generic Drug Entry Prior to Patent Expiration: An FTC Study (July 2002), at iii, <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>.
19. *Buspirone Antitrust Litig.*, 185 F. Supp. 2d 363 (S.D.N.Y. 2002).
20. The *Noerr-Pennington* Doctrine developed from three Supreme Court cases: *Eastern R.R. Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127 (1961); *United Mine Workers of Am. v. Pennington*, 381 U.S. 657 (1965); and *California Motor Transp. Co. v. Trucking Unlimited*, 404 U.S. 508 (1972).
21. BMS and Watson have apparently settled on terms that include a \$32 million payment by BMS to Watson. See F-D-C Reports (The Pink Sheet), April 8, 2002, at 25.
22. *Buspirone*, 185 F. Supp. 2d at 371.
23. Agreement Containing Consent Order, Biovail Corp. (No. 011 0094) (Apr. 23, 2002), available at <http://www.ftc.gov/os/2002/04/biovaildecision.htm>.
24. Federal Trade Commission, Generic Drug Entry Prior to Patent Expiration: An FTC Study (July 2002), <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>.
25. *Id.* at v.
26. *Id.* at 50 (emphasis in original).
27. Interestingly, with respect to polymorph patents, the report notes that an NDA holder is generally restricted to selling only the precise polymorph that was approved in the NDA but that, for purposes of filing an ANDA, a different polymorph is deemed by the FDA to be the same as the polymorph approved in the NDA. *Id.* at A-41.
28. The report states that questions about listing are also raised by patents that claim a drug by the process by which it is prepared (i.e., product-by-process patents) and by patents that constitute double-patenting, because they claim subject matter that is obvious in view of the claims of another patent. *Id.* at 52.
29. 67 Fed. Reg. 65,447 *et seq.* (2002) (to be cited at 21 C.F.R.) (proposed Oct. 24, 2002).
30. S. 812 also contains provisions that would permit pharmacists and wholesalers to import drugs from Canada.
31. S. 812, § 104(a)(1)(A)(ii).
32. 21 C.F.R. 314.52(a)(3), as proposed. The rationale for the reinterpretation is explained at 67 Fed. Reg. at 65,454-65,456 (2002).
33. S. 812, § 103(a)(2)(C); 21 C.F.R. 314.53(c), as proposed.
34. 21 C.F.R. 314.53(b), as proposed.
35. The term "polymorph" refers to the particular size and shape of a given pharmaceutical compound when the compound is in crystalline form.
36. Interestingly, the FDA characterizes the recognition that patents on different forms of an approved drug substance should be listed (if the different form is the "same" as the approved drug substance) as "a change from our previous position." 67 Fed. Reg. at 65,453 (2002). In fact, however, the FDA had previously taken this same position. See, e.g., letter from Janet Woodcock, MD, to Messrs. Moore *et al.*, Nov. 21, 2000, Docket No. 00P/0499/CP1, especially n.6.
37. S. 812, § 103(a)(2)(E).
38. Comments on the proposed rulemaking were due on December 24, 2002.

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This is Part II of a two-part article. Part I, which appeared in the March 2003 issue of The Licensing Journal, provided background on the legal framework for approval of generic drugs, on lifecycle management strategies employed by research-based pharmaceutical companies to protect their innovation, and issues that have resulted from the statutory requirement that pharmaceutical companies list patents that cover their approved drugs in the FDA's "Orange Book."

Over the last few years, the Federal Trade Commission (FTC), state, and private plaintiffs have filed a number of antitrust cases challenging patent settlement agreements between pioneer companies and would-be generic entrants. The first cases involved interim settlements in lieu of preliminary injunctions, by which the generic firm, in exchange for a substantial monetary payment, agreed not to enter the market pending resolution of the patent infringement suit. More recently, the FTC has challenged (so far unsuccessfully) a final settlement whereby the generic firm agreed not to enter the market for a period of time shorter than patent life but longer than would be the case if the generic firm successfully defended the infringement action. In both situations, the 180 day exclusivity period magnified the effect of the agreements because subsequent generic entrants could not

have their abbreviated new drug applications (ANDAs) approved until either (1) the first generic firm began to market its product, or (2) a subsequently-filing, would-be entrant successfully defended an infringement suit (which might be concluded later than the first-filing generic's suit would have been resolved) and allowed the first ANDA filer's 180-day exclusivity to run. Consequently, if the first ANDA filer delayed its entry pursuant to an agreement with the pioneer company, subsequent generic entry might also be delayed.

This discussion begins by summarizing the FTC and private enforcement actions, then analyzes some of the difficult and unresolved issues inherent in those enforcement actions, and concludes by discussing the FTC industry study and its recommendations.

FTC Enforcement Actions

In the first of three administrative actions, on March 16, 2000, the FTC filed an administrative complaint¹ against Hoechst Marion Roussel (HMR) (which subsequently merged with RhonePoulenc-Rorer to form Aventis S.A. (Aventis)) and Andrx Corporation (Andrx), alleging violations of Section 5 of the Federal Trade Commission Act.

In September 1995, Andrx filed an ANDA seeking approval to market a generic version of Cardizem, HMR's blockbuster cardiovascular drug. The ANDA included a paragraph iv certification as to the HMR patents listed in the Orange Book. Andrx's paragraph iv certification precipitated a patent infringement suit by HMR on January 31, 1996.

In January 1997, Purepac Pharmaceutical Co., (Purepac) filed a second ANDA for diltiazem with a paragraph iv certification. HMR promptly sued Purepac for patent infringement.

In June 1997, Biovail also filed an ANDA with a paragraph iv certification. Biovail and HMR had already settled a legal dispute² on terms including that HMR would not sue Biovail for patent infringement based on Biovail's efforts to launch products containing diltiazem. Nevertheless, under the heading of "Anticompetitive Conduct," the complaint alleges that HMR offered to pay Biovail to assist in the develop-

ment of another product if Biovail would refrain from selling generic diltiazem until at least July 1999.

On September 24, 1997, HMR and Andrx entered into an agreement under which Andrx agreed not to market the generic diltiazem for which it was seeking approval (or any other generic diltiazem product) until the litigation was finally resolved or until HMR authorized Andrx or any other party to sell a generic diltiazem. Andrx also agreed to maintain its ANDA and not to relinquish its 180-day exclusivity period. In exchange, HMR agreed to pay Andrx \$10 million per quarter commencing with approval of Andrx's ANDA. In addition, HMR granted Andrx an option to acquire a royalty-bearing license under HMR's intellectual property rights in diltiazem, the royalty rate being dependent on the outcome of the patent infringement litigation.

The FTC reached a consent agreement with both HMR and Andrx on April 2, 2001. Under the terms of the Decision and Order,³ HMR and Andrx agreed that they:

1. Would not enter into any agreement between a NDA holder and an ANDA first filer under which the ANDA first filer is prohibited from (or penalized for) relinquishing its 180 day exclusivity period;
2. Would not enter into any agreement between a NDA holder and an ANDA first filer under which the ANDA first filer agrees not to commercialize a product that is not the subject of patent infringement litigation; and
3. Would not enter into any agreement between a NDA holder and an alleged infringer under which the parties agree not to dismiss a patent infringement litigation and the NDA holder provides anything of value to the alleged infringer and the alleged infringer agrees not to sell the product at issue during the litigation (except pursuant to a joint stipulation if the Court and the FTC are advised of the proposed agreement).

On the same day the complaint against Aventis and Andrx was filed, the FTC, on March 16, 2000, accepted for public comment a proposed settlement of a complaint against Abbott Laboratories (Abbott) and Geneva Pharmaceutical Corporation (Geneva), a generic subsidiary of Novartis, alleging violations of Section 5 of the Federal Trade Commission Act.⁴ The consent order was made final on May 22, 2000. The relevant facts, according to the complaint,⁵ are as follows.

Around January 1993, Geneva filed an ANDA seeking approval to market a generic version of Hytrin tablets for treatment of benign prostatic hypertrophy. In about December 1995, Geneva filed a second ANDA for the capsule form of the drug. In 1996, Abbott listed a new patent in the Orange Book. In April 1996, Geneva submitted a paragraph iv certifi-

cation that neither its capsule nor its tablet would infringe the claims of the newly-listed patent or any of Abbott's other listed patents. On June 4, 1996, Abbott sued Geneva for patent infringement based on Geneva's terazosin HCL tablet but asserted no claim against Geneva's capsule.

According to the complaint, Geneva received FDA approval to market its generic capsules on March 30, 1998, and promptly approached Abbott with an announcement of its intent to launch unless Abbott would pay Geneva to stay off the market. On April 1, 1998, Abbott and Geneva entered into an agreement under which Geneva would not market any generic terazosin capsule or tablet until the earlier of: (1) the final resolution of the patent infringement litigation involving Geneva's terazosin HCL tablet product, including review through the Supreme Court; or (2) entry of another generic terazosin HCL product. Geneva also agreed not to transfer or relinquish its 180-day exclusivity period.

As part of the agreement, Abbott agreed to pay Geneva \$4.5 million per month until a District Court judgment. If the District Court found noninfringement, Abbott would thereafter place the monthly payments into an escrow account until final resolution. The party who ultimately prevailed in the litigation would receive the escrowed money.

The Court in which the patent litigation was pending was not made aware of the agreement. In September 1998, the District Court ruled that the patent was invalid. This decision was affirmed by the Federal Circuit in July 1999. In August 1999, the parties terminated their agreement and Geneva launched its generic capsules.⁶

The parties settled the administrative action on terms that were substantially the same as those set out in the Decision and Order in the Aventis-Andrx case.⁷

On the date on which the consent agreement between the FTC and Aventis and Andrx was announced, April 2, 2001, the FTC filed an administrative complaint⁸ against Schering-Plough Corporation (Schering), American Home Products (AHP) (now Wyeth), and Upsher-Smith Laboratories (Upsher-Smith), alleging violations of Section 5 of the Federal Trade Commission Act. The relevant facts, according to the complaint, are similar in some respects to those of the preceding FTC actions.

On August 5, 1995, Upsher-Smith filed an ANDA, with a paragraph iv certification, for a generic version of K-Dur extended release potassium chloride tablets and capsules. Schering, the NDA holder sued for infringement of its patent, which expires September 6, 2006. On the eve of trial, June 17, 1997, the parties settled the patent infringement litigation.

Under the terms of the settlement, Schering paid \$60 million to Upsher-Smith; Upsher-Smith agreed not to market any generic version of K-Dur (whether or not infringing) until September 2001. The parties

stipulated to dismissal of the lawsuit and Schering received licenses to market five Upsher-Smith products (which, according to the FTC, were of minimal or no value to Schering).

On December 29, 1995, AHP filed an ANDA with a paragraph iv certification, which also precipitated a patent infringement suit by Schering. In about January 1998, the parties settled on terms similar to the Schering/Upsher-Smith settlement. Schering agreed to pay \$30 million to AHP; AHP agreed not to market any generic version of K-Dur until January 2004 and to market no more than one generic version between January 2004 and September 2006. The monetary payment was based on certain milestones and licenses to market two AHP products (which, according to the complaint, did not have significant value to Schering).

Andrx filed an ANDA in June 1999, but was not sued by Schering. According to the FTC complaint, Andrx could not market its product until expiration of Upsher-Smith's 180-day exclusivity period.

On February 19, 2002, the FTC and AHP reached a proposed consent agreement.⁹ Schering-Plough and Upsher-Smith proceeded to trial, however, and after considering the evidence, the Administrative Law Judge (ALJ) dismissed the FTC's complaint. The FTC's Complaint Counsel had argued that the agreements not to enter until a specified date constituted a "temporal market division" and that the licenses of products from Upsher-Smith and AHP to Schering were shams to cover up "reverse payments" made to induce the generic manufacturers to delay entry of their products onto the market. Complaint Counsel argued that such market divisions and "reverse payments" should be condemned as *per se* unlawful, after a "quick look" rule of reason analysis or, at a minimum, after a full rule of reason analysis.

The ALJ rejected the *per se* analysis, distinguishing the two federal district court cases (*Cardizem* and *Terazosin*) that had applied a *per se* rule to agreements between pioneer companies and generic companies under which the former paid the latter not to enter the market until after the underlying patent litigation had been fully resolved. The ALJ concluded that those cases were distinguishable because they involved interim, rather than final, settlements of litigation and because they did not permit the generic companies to market their products before patent expiration.¹⁰

The ALJ further rejected the "quick look" approach, reasoning that the anticompetitive effects were not intuitively obvious because Upsher-Smith and AHP might not have entered the market until the expiration of Schering's patent and indeed might not have entered at all.

Finally, the ALJ ruled that Complaint Counsel failed to meet its burden of proof as to a rule of reason violation or a monopolization theory, on the grounds (among others) that:

- Complaint Counsel failed to prove a relevant product market limited to 20 mEq extended release potassium chloride supplements and that, in a broader market for all potassium chloride supplements, Schering lacked market power;
- A patent should be presumed valid; Complaint Counsel had failed to show that the Schering '743 patent was invalid; if valid, the patent itself would have prevented competition; and therefore Complaint Counsel had failed to show there was any competition to be restrained;
- Complaint Counsel had failed to prove that the generic firms would have entered prior to resolution of the patent suits; and
- Complaint Counsel had failed to prove that the payments were for delay and not for products licensed by the generic companies to Schering.

The case is now on appeal to the Commission.¹¹

Private Enforcement Actions

Andrix v. Biovail, 256 F3d 799 (D. Col. 2001)

This case originated out of Andrx's challenge to an FDA regulation that conditioned a period of market exclusivity on the successful defense of a patent infringement action. Andrx sought an order directing the FDA to withdraw its approval of an ANDA that authorized another company, Mylan Pharmaceuticals, to market a generic version of a drug that Andrx believed it was entitled to market exclusively for 180 days. The Court granted Andrx's motion for a temporary restraining order against Mylan. Subsequently, the Court of Appeals for the District of Columbia ruled similarly in a different case on the same issue.¹² The FDA subsequently issued new guidelines to comport with the Court rulings. The only remaining issue before the Court was a counterclaim filed against Andrx by Biovail, alleging that the diltiazem settlement agreement violated Sections 1 and 2 of the Sherman Act.

The DC District Court took a fundamentally different view of Biovail's claims than did the Court in New Jersey, as discussed subsequently.¹³ The DC District Court concluded that Biovail did not establish antitrust standing because it did not show the requisite causal connection between its alleged injury and the alleged antitrust violation. The Court found that because Biovail did not have FDA approval, any loss of potential sales was either only marginally related or wholly unrelated to the agreement reached between HMR and Andrx. The Court also noted that even if it invalidated the agreement, Andrx could choose not to market its product, a result which is within the statutory scheme of the Hatch-Waxman Act (HWA). Thus, the Court stated that "[a]t least

some of the potential delay in the marketing of generic versions of Cardizem, then, is more directly caused by the statutory scheme than by any agreement between Andrx and HMRI.¹⁴

The Court further elaborated that "[t]he reason Biovail cannot enter the market is because of the existence of a troublesome statutory scheme that prohibits it from marketing a drug until the first ANDA recipient goes to market, and which places no restrictions on when, or even whether, that applicant must go to market."¹⁵ The Court also noted in a footnote that in the *Mova* decision, the Court of Appeals referred to the Andrx/HMR agreement when it considered the separate issue of the successful defense condition to 180-day exclusivity, and stated the potentiality that "the first applicant could even collude with the original patent holder to prolong their litigation, and thereby keep the second applicant's drug off the market indefinitely."¹⁶ In addition, the Court concluded that Biovail's alleged injury (delay in sales) was speculative, because there was no evidence that, absent the agreement, Biovail could have marketed its product (noting that Biovail had not yet attained FDA approval).

The DC Circuit Court of Appeals found that the District Court correctly dismissed Biovail's antitrust claim but should have granted the dismissal without prejudice to allow Biovail an opportunity to replead. The DC Circuit stated that because Biovail "did not explicitly allege that it was prepared to bring a generic version of Cardizem CD to the market or that it anticipated FDA approval," there were no facts to support its claim of injury from the agreement.¹⁷ However, in its motion for reconsideration, Biovail alluded to facts, including the FDA approval and the intent to enter the market, that could have entitled it to relief. Thus, the DC Circuit found that Biovail may be able to cure its pleading deficiency.

Biovail Corporation International v. Hoechst A.G., 49 F.Supp. 2d 750 (D.N.J. 1999)

The history of battles by Aventis and its predecessor companies with generic drug manufacturers trying to launch generic versions of Aventis' blockbuster drug, Cardizem (diltiazem), is worthy of a law school exam.¹⁸ It begins with an alliance between Biovail and Hoechst-Roussel Pharmaceuticals (HRP) in which the parties were collaborating on the development of their own branded version of diltiazem, Tiazac, to compete with Cardizem, which was then manufactured by Marian Merrell Dow (MMD). After HRP merged with MMD, the new company, HMR, terminated the alliance with Biovail. Biovail sued for breach of contract. HMR and Biovail settled that litigation under terms that included that HMR would not contest Biovail's continuing development of diltiazem.

In addition, the FTC, as a condition for approval of the HRP-MMD merger, required HMR to grant to Biovail the right to cross-refer to certain data in the Cardizem NDA file for purposes of gaining approval for the Tiazac NDA, "including any supplemental NDAs or related NDAs." HMR subsequently informed the FDA that the right of reference was limited to the Tiazac NDA or to any NDA for the same formulation of diltiazem.

As a result, when Biovail modified the Tiazac formulation and submitted a NDA for the new formulation, the FDA refused to accept the application because it relied on data in the Cardizem NDA for which Biovail did not have the right to cross-refer. Biovail then switched tactics and filed an ANDA, with a paragraph iv certification. Unfortunately for Biovail, Andrx had already entered the fray by filing an ANDA for its generic version of diltiazem, thus making Andrx the first to file an ANDA for generic diltiazem with a paragraph iv certification and giving Andrx the benefit of the 180-day exclusivity period. HMR sued Andrx for patent infringement. HMR and Andrx then entered into a settlement agreement under which Andrx would not launch its generic during pendency of the litigation and HMR agreed to pay Andrx \$10 million per calendar quarter.

Biovail now found itself blocked. It was unable to gain approval of either an NDA, because it lacked access to required safety and efficacy data, or an ANDA, because Andrx had the 180-day exclusivity period. Biovail sought relief from the Courts, charging that HMR violated Sections 1 and 2 of the Sherman Act by:

1. Interfering with FDA's acceptance of Biovail's NDA;
2. Settling with Andrx on terms that kept Andrx's generic off the market;
3. Interfering with Canadian approval of Biovail's diltiazem by raising "specious" safety and bioequivalence concerns with the Canadian authorities;
4. Raising "similar bogus concerns" through its sale representatives;
5. Publicly threatening Biovail with patent infringement litigation; and
6. Attempting to reach agreement with Biovail on terms that would have delayed launch of Biovail's generic.

The antitrust injuries alleged by Biovail included exclusion from the market and damages to its share price. The reported decision and opinion relate to HMR's motion to dismiss on the grounds that none of the particular acts complained of were shown to have caused antitrust injury to Biovail. The Court denied HMR's motion, stating that the proper test is whether Biovail suffered antitrust injury as a result of the alleged violations viewed collectively, not singly.

With respect to the settlement agreement with Andrx, The Court stated,

[I]t is clear to this Court that a reasonable trier of fact could conclude that an agreement between two competitors to delay the applicability of an exclusivity period for the purpose of keeping another competitor out of the market is an unreasonable restraint of trade or willful attempt to maintain or obtain a monopoly.¹⁹

The Court also rejected HMR's argument that Biovail was simply expressing frustration with the statutory scheme. According to the Court, "Biovail's claim reflects its contention that defendants are taking advantage of the exclusivity period in an anticompetitive manner."²⁰

Zeneca v. Pharmachemie B.V., 37 F. Supp. 2d 85 (D. Mass.1999)

In the patent infringement action brought by Zeneca²¹ (now AstraZeneca) alleging infringement of its patents relating to Nolvadex[®] tamoxifen, the defendant, Pharmachemie, raised several affirmative defenses aimed at invalidating the patent and/or rendering it unenforceable based on a previous unfavorable District Court decision that Zeneca's tamoxifen patent was unenforceable²² and on Zeneca's actions settling the litigation. Zeneca moved for partial summary judgment on three of its affirmative defenses: (1) collateral estoppel; (2) patent misuse; and (3) unclean hands. These affirmative defenses were at issue before the Court.

Regarding patent misuse, the judge stated that the conduct at issue was not one of the practices that had been deemed to constitute *per se* patent misuse. The judge stated that Zeneca had not "somehow broadened the physical scope of the '516 patent," rejecting Pharmachemie's argument that Zeneca had expanded the applicability of the patent because Zeneca's "'collusive' settlement agreements with Barr . . . 'revived' its rights [in the patent that might otherwise have been invalidated] and bought an extension of the '516 patent by ensuring the vacatur of the District Court judgment by the Federal Circuit." Reasoning that "Pharmachemie's analysis would apply to every case that was settled while on appeal," a magistrate judge concluded that as a matter of law the conduct alleged "does not fall within the rubric of patent misuse."²³

Regarding collateral estoppel, the judge stated that Pharmachemie had conceded that Zeneca was not bound by collateral estoppel because the unfavorable District Court decision had been vacated after the settlements were reached.

The judge also rejected Pharmachemie's argument that Zeneca's settlements with Barr after the Court ruling of unenforceability fell within the scope of the doctrine of unclean hands. The judge relied on a report and recommendation filed by a magistrate

judge, which stressed that Zeneca's settlement payment and vacatur of the District Court opinion were consistent with Federal Circuit practice and asserted that the conduct alleged did not rise to a sufficient level of unconscionability. The Court suggested that "none of [Zeneca's] conduct is intrinsically wrong or inequitable as is bribery or perjury," and that "something more" than the showing required for inequitable conduct (which Pharmachemie had asserted in its first affirmative defense) would be necessary.²⁴

Coat Tail Cases

The list of "coat tail" matters is long and lengthening. Among the most interesting of these are actions brought by various types of plaintiffs against Aventis and Andrx based on their settlement of the diltiazem patent litigation and against Abbott, Geneva, and Zenith based on their settlement of the terazosin patent litigation. In both these cases, the District Courts in which the cases were consolidated found that the agreements are *per se* illegal.

In the diltiazem case, various indirect purchasers of Cardizem (diltiazem), wholesalers, and drug store and supermarket chains brought multiple suits against Abbott, Geneva, and Zenith, alleging violations of Section 1 of the Sherman Act and various state antitrust and unfair competition statutes. The cases have been consolidated in Michigan for pretrial processing and the District Court has been presented with numerous motions.

Among the motions brought by Plaintiffs was a motion for summary judgment that the Aventis/Andrx agreement is a horizontal market allocation agreement and is therefore *per se* illegal.²⁵ This motion was granted by the Court notwithstanding the defendant's arguments that (1) the agreement is not between actual or potential horizontal competitors; (2) does not allocate markets or fix prices and thus does not fall within the category of business practices analyzed under the *per se* rule; (3) is not a "naked" restraint of trade but rather an agreement that was reasonably ancillary to procompetitive activity; and (4) is analogous to a patent settlement and thus should be analyzed under the rule of reason.

Among the issues addressed by previous motions is whether *Noerr-Pennington* immunized Aventis from antitrust liability.²⁶ The Court found that *Noerr-Pennington* did not apply because there was no claim of anticompetitive harm resulting from the incidental effects of a publicity campaign, but rather the source of the anticompetitive harm was a private market allocation agreement between competitors. The Court also found that the agreement did not fall within conduct "reasonably and normally attendant on litigation" that would otherwise be immunized from antitrust liability.²⁷ In addition, other courts have observed that private settlement agreements may result in antitrust liability "when they are attended by anticompetitive results."²⁸

In the same reported opinion, in view of its decision with regard to immunity, the Court further considered whether the Aventis/Andrx patent litigation was a sham. The Court found that the plaintiffs did not meet the burden of the two-prong test for determining a sham,²⁹ but it would allow the plaintiffs to amend their complaints to adequately plead facts supporting a sham. The Court also found that the plaintiffs sufficiently pled antitrust injury because, even though the Aventis/Andrx submitted additional plausible and legally permissible explanations as to why Andrx prolonged entering into the market, there was still a causal connection between the Aventis/Andrx anticompetitive conduct and the alleged injuries.

Furthermore, the Court found that compliance with the HWA did not provide immunity from the antitrust laws. In its discussion, the Court stated that the HWA did not authorize Aventis to contract with and pay Andrx to postpone its entry into the market beyond the time permitted by the HWA. In addition, the FDA had recently observed, in a preamble discussion to proposed regulations, that agreements "between a patent holding drug company and a first-to-apply generic drug company 'may contribute to delayed generic competition by forestalling the beginning, or triggering, of the 180-day exclusivity period.'"³⁰

Finally, in regard to the state claims, the Court found that Aventis/Andrx's conduct significantly and adversely affected trade and commerce and was cognizable under state law (Wisconsin and Tennessee). The Court also found that because Aventis took actions that constituted transactions of business and such actions caused an injury in those states, a *prima facie* case of personal jurisdiction was established.

In the terazosin case, various plaintiffs brought actions against Abbott alleging that its agreements with Geneva and Zenith violated Section 1 of the Sherman Act. In response to motions filed by the plaintiffs, the Court granted partial summary judgment and found that the agreements were *per se* Sherman Act violations.³¹ The Court based its decision on that fact that the agreements illustrated that Geneva and Zenith "foreswore competing with Abbott . . . for terazosin hydrochloride drugs and promised to take steps to forestall others from entering that market for the life of their respective agreements in exchange for millions of dollars in monthly or quarterly payments."³² The Court found that "[t]his scheme of agreements clearly 'denied to consumers the opportunity to choose among alternative offers without offering the possibility of any joint, efficiency-producing activities.'"³³ Furthermore, the forestalling by Geneva and Zenith of competition for sales of terazosin hydrochloride drugs, which was a horizontal territorial limitation, the Court found, was "one of the classic examples of a *per se* violation."³⁴

The case is now before the Eleventh Circuit on interlocutory appeal.³⁵

Implementation of lifecycle management strategies by pharmaceutical companies has given rise to numerous additional lawsuits by various plaintiffs, e.g., consumer groups and state attorneys general, usually as "follow-ons" to FTC investigations or litigations between affected competitors. For example, there are apparently at least 16 actions against Schering, Upsher-Smith, and AHP following the FTC action against these companies.³⁶ Included among these are cases brought by the Prescription Access Litigation Project (PALP)³⁷ and the New York City Patrolmen's Benevolent Association (PBA).³⁸

Bristol-Myers Squibb's (BMS) actions in defense of market exclusivity for BuSpar have resulted in at least four patent disputes, 22 antitrust actions, and 12 "coat tail" cases.³⁹ The plaintiffs are, variously generic drug makers who seek or have sought to enter the buspirone market, direct purchasers of buspirone products, end-payers who have purchased buspirone, consumer organizations, or their representatives, and 30 states. All complaints, except those filed by the states, asserted that BMS conspired to restrain trade in the buspirone market by settling a patent infringement suit with Danbury Pharmacal, Inc. and its affiliate, Schein, in 1994.⁴⁰ The Court dismissed such claims by generic drug makers based on the four year statute of limitations⁴¹ but allowed the claims by purchasers to stand to the extent that they are predicated on purchases of BuSpar beginning four years prior to the filing of their complaints.

In May 2001, Andrx was sued by the state attorneys general of New York and other states for antitrust violations in connection with its agreement with Aventis concerning Andrx's generic diltiazem. On September 25, 2001, Colorado, Kansas, and Florida filed a lawsuit in the US District Court for the Southern District of Florida against Abbott, Ivax Pharmaceuticals (Ivax), and Geneva.⁴² The complaint alleges that Abbott and Ivax entered into an agreement similar to the Abbott/Geneva agreement. Colorado, Kansas, and Florida allege that Abbott filed 17 patent infringement suits against generic drug manufacturers from 1993 to 1998 and that these suits were used by Abbott "as an anti-competitive weapon."⁴³

Barr recently reported that it was served with a civil investigative demand from the Oregon attorney general's office for information regarding its settlement of a patent challenge with AstraZeneca regarding tamoxifen.⁴⁴ (On the other hand, in December 2001, Barr announced that it was notified by the Texas Office of the Attorney General that the state's investigation into the ciprofloxacin settlement agreement was closed.)⁴⁵ Meanwhile, AstraZeneca and Barr are defending suits from various plaintiffs, including the PBA and PALP.⁴⁶

The PBA has also sued Pfizer and Mylan based on an agreement between the parties relating to Procardia[®] extended-release nifedipine, Pfizer's hypertension and angina drug.⁴⁷ Under the terms of that

agreement, it appears that the litigation was dismissed and Mylan was authorized to sell generic extended-release nifedipine manufactured by Pfizer.⁴⁶

PALP is currently involved in multiple other actions against pharmaceutical companies for allegedly unlawful tactics, including cases involving Augmentin[®] amoxicillin-sodium clavulanate, Claritin[®] loratidine, Neurontin[®] gabapentin, Relafen[®] nabumetone and Remicade[®] infliximab.⁴⁹

Discussion: The Problem of Uncertainty

The range of outcomes and approaches in these cases is startling. The district courts in *Cardizem* and *Terazosin* condemned the agreements as *per se* unlawful market divisions. Two FTC Commissioners, in speeches explaining their approach to these cases, have identified several “red flags” that appear to give rise to a kind of presumptive unlawfulness characteristic of a “quick look” approach. An FTC ALJ, in the *Schering-Plough* case, firmly rejected both the *per se* rule and the “quick look” approach in favor of a full-blown rule of reason, with the burden on Complaint Counsel to prove, among other things, that the patent was invalid and that the generic firms would have entered prior to resolution of the patent suits.

What accounts for this vast disparity? We think that the FTC and the courts have struggled so hard with these cases because, unlike most other forms of property, the boundaries and, even the existence, of the property right can be highly uncertain. Fundamental to the notion of a restraint on competition is that there be competition to restrain. In the case of intellectual property, this cannot be resolved simply by looking to see whether two sellers are selling the same product. Instead, as the joint Department of Justice and FTC Antitrust Guidelines for the Licensing of Intellectual Property⁵⁰ observe, there is competition between the parties to restrain only if both parties would have sold the product without needing a license between them.⁵¹ If the scope and validity of the patents owned by one or both of the parties is uncertain, then it may not be known, either by the parties at the time of the conduct or by the court at the time of hearing an antitrust challenge, whether the parties are horizontal competitors or not.

As noted previously, both *Cardizem* and *Terazosin* condemned the defendants’ conduct as *per se* unlawful. As the court in *Terazosin* saw it:

Geneva and Zenith foreswore competing with Abbott in the United States market for terazosin hydrochloride drugs . . . in exchange for millions of dollars . . . Under this scheme, the defendants would earn their profits by limiting marketwide output and maintaining a higher price for Abbott’s product.

Abbott’s agreements with Geneva and Zenith to forestall competition in the United States for sales of terazosin hydrochloride drugs confront the Court with “one of the classic examples of a *per se* violation”—“an agreement between competitors at the same level of the market structure to allocate territories in order to minimize competition.”⁵²

Both the *Cardizem* and *Terazosin* courts were serenely untroubled by the fact that the relationship between two parties to a transaction is horizontal only if there would have been competition between those parties absent a license between them. Effectively, they did not even ask this crucial question. There are problems with this “don’t ask, don’t tell” approach, however. The IP Antitrust Guidelines did not pull the standard for identifying horizontal arrangements out of a hat; it came from basic antitrust principles about the conditions under which one firm exerts competitive force on another to the benefit of consumers. If one firm can lawfully be in the market only at the sufferance of the other, the competitive relationship between them is simply different from that between two ordinary competitors. If the patent holder refuses to permit the competition, and the other firm enters anyway, the other firm is a thief; if the patent holder does permit the competition, the other firm is a distributor.

If it is a thief, then not only is the competition unlawful, but Congress has made a judgment that allowing the competition is not a benefit to consumers, but instead results in a long-term efficiency loss. The Constitution empowers Congress to enact a patent law in order to “promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁵³ The implicit bargain is that the short-term loss in static allocative efficiency will be more than offset by the gain in dynamic efficiency.⁵⁴

If the firm is a distributor, we should be no more comfortable about courts blithely mistaking it for a horizontal competitor in the intellectual property context than we are in the context of tangible property. True, that very issue perplexed the antitrust profession for many years under the rubric of “dual distribution.” When a manufacturer sells both through independent distributors and directly to consumers in apparent competition with those distributors, courts struggle over whether the relationship is horizontal or vertical.⁵⁵ More recently, however, it has become customary, and properly so, to think of such relationships as vertical.⁵⁶ The terms on which a manufacturer, who also distributes, sells to an independent distributor has a profound effect on how much of a competitive force the distributor exerts, and if the manufacturer did not sell its product to the independent distributor, it would not be a competitor at all.

Thus, the distributor's influence has more to do with arbitraging away potential price discrimination than with true competition. As concern with price discrimination has faded, particularly in the intellectual property context,⁵⁷ so too has the tendency to mistakenly analyze such relationships as horizontal.

In short, we cannot, consistent with modern antitrust principles, classify the parties as horizontal competitors unless we know that they likely would have competed lawfully absent a license between them. Courts must ask and tell if the parties to an accused settlement are indeed horizontal competitors.

One option, therefore, would be to inquire, as a factual matter, whether the patents owned by one or both parties would have blocked the other from competing. Like Russian dolls, the antitrust case opens up to reveal that a full-scale intellectual property litigation hides inside. The FTC did this in a case involving patents on the use of an excimer laser for vision correction, *Summit-VISX*,⁵⁸ and, as noted, the ALJ ruled in *Schering-Plough* that Complaint Counsel bears the burden of proving that the patents in question are invalid or not infringed. The Eleventh Circuit may do the same in deciding the interlocutory appeal in the terazosin case.

This is a significant advance over the "don't ask, don't tell" approach, but there are three basic problems. First, it is extraordinarily resource-intensive. The FTC spent considerable time in pretrial, trial, and post-trial in *VISX* on the issues of fraudulent and inequitable conduct in procurement of the patent alone. (Issues of whether the patent was invalid or not infringed for other reasons, or whether other firms could have invented around the patent were no longer in the case because allegations against the pooling agreement that settled disputes between *VISX* and *Summit* had been settled.) Second, by definition, trying this issue eliminates the principal efficiency that most settlements are designed to achieve—the early and permanent resolution of disputes with a minimum of resources. Third, it is more than a little problematic to tell parties that if they are uncertain whether the patents in question are valid and infringed or not, they can settle the case, but their conduct in so doing might be illegal if it later turns out that the patents were invalid or not infringed.⁵⁹

A more pragmatic approach might be to identify particular characteristics of settlements that would make them more or less suspect. For example, FTC Commissioner Thomas B. Leary has suggested that it would be lawful to enter into a "straightforward settlement" in which the NDA holder grants a royalty-free license permitting the ANDA filer to launch on a future date that is before patent expiration and that reflects "the parties' assessments of their legal positions, their risk tolerance, and other business factors."⁶⁰

This is the basis on which Barr has defended its ciprofloxacin and tamoxifen settlements.⁶¹ For exam-

ple, an April 2, 2001, press release on ciprofloxacin by Barr states, in part,

Our decision to settle the patent challenge assures that consumers have access to a more affordable generic ciprofloxacin at least six months ahead of the patent expiry," said Bruce L. Downey, Barr's Chairman, and CEO. "There was no assurance that Barr's patent challenge could have succeeded in the Courts. This settlement represents a substantial savings on a product with current annual brand sales in excess of \$900 million." The patents protecting ciprofloxacin run through December 2003.

It is also important to note that our settlement of the ciprofloxacin patent challenge does not preclude any other pharmaceutical company from filing its own challenge to the product," Downey continued. "In fact, another company, which had challenged the patents protecting ciprofloxacin, has lost at the District Court level."⁶²

Following the filing of the suit by PALP concerning the tamoxifen settlement, Barr issued a press release stating, in part,

As a result of our patent settlement, breast cancer patients have had access to a more affordable version of Tamoxifen years earlier than they would have if we had pursued our challenge and failed," said Bruce L. Downey, Barr's Chairman and CEO. The Company distributes its product to drug stores, distributors and wholesalers at approximately 15 percent less than the brand price.

The validity of this settlement, and its value to consumers, is obvious," Downey continued. "Our decision to settle the case has given women a lower cost alternative to the brand product. When we settled the case, we believed that there was a very real possibility that we might have lost when the innovator appealed our District Court decision. In fact, subsequent challenges by other companies have failed, confirming that we made the right decision. If we had not settled, and had lost on appeal, nearly a decade of multi-million dollar savings would never have been realized by consumers."⁶³

Conversely, the FTC actions in the terazosin, diltiazem, and potassium chloride cases make it clear that certain provisions of patent infringement litigation settlement agreements signal the potential for trouble with the FTC:

1. Reverse payments (*i.e.*, payments by the NDA holder to the ANDA filer) in consideration for which the ANDA filer agrees to delay market entry;
2. Absence of judicial review; and
3. Ancillary restrictions, *e.g.*, an agreement not to market non-infringing products or an agreement not to transfer or relinquish the 180-day exclusivity period.

FTC Commissioner Sheila F. Anthony has referred to such provisions as "red flags" in patent litigation settlement agreements between NDA holders and ANDA filers.⁶⁴ Similarly, while Commissioner Leary stopped short of opining that reverse payments in exchange for delayed market entry are *per se* illegal, he noted that he is "tempted to support a presumption that reverse payments are illegal," but, pending further study, he is holding "extreme skepticism" about such payments, acknowledging that it is conceivable that there may be instances when reverse payments can be justified.

These kinds of "red flags" are useful in establishing a forward-looking rule as is typically the FTC's task in cases under Section 5 of the Federal Trade Commission Act.⁶⁵ Care must be exercised, however, in applying such rules retrospectively in private actions seeking enormous treble damages. In the pharmaceutical industry context, the alleged infringer typically has not yet marketed a product. Its alleged "infringement" is somewhat artificial and created by the HWA⁶⁶ to facilitate early resolution of patent disputes. In such a case, it is not surprising that no money flows from the alleged infringer to the patentee. "Reverse payments," suggesting that there is something abnormal or unexpected about the direction of payment, may thus be an unduly inflammatory characterization. Moreover, it is not true that payments never flow from the patentee to the alleged infringer. If a court were to issue a preliminary injunction preventing the alleged infringer from making, using, or selling the disputed product pending the outcome on the merits, the patentee seeking that injunction would be required to post a bond. If the patentee ultimately lost on the merits, those monies would be used to compensate the alleged infringer for the harm it suffered during the pendency of the litigation. Furthermore, even without a formal court ruling, it is common for parties to enter into standstill agreements that are the functional equivalent of preliminary injunctions. Indeed, many judges routinely encourage or even press the parties to enter into such agreements to obviate the need for the court to rule. If, therefore, the parties were to agree to a standstill agreement or a stipulated preliminary injunction that kept the alleged infringer off the market and provided for an escrow fund to be paid to the alleged infringer if it prevailed on the merits, and nothing more, it

would be hard to infer anything untoward from the mere direction of the flow of funds.

The FTC considered this analogy and Commissioners Anthony and Leary have explained how they distinguished it. In a speech to the ABA, on June 1, 2000,⁶⁷ Commissioner Anthony distinguished the reverse payments and delayed launch provisions of the Abbott/Geneva agreement from a stipulated preliminary injunction on the following bases:

1. A preliminary injunction lasts only as long as litigation at the trial Court level whereas the agreement extended through appeals to the Supreme Court;
2. While a preliminary injunction may require posting of a bond, the payments by Abbott to Geneva were not contingent on success by Geneva (and, apparently, exceeded Geneva's lost profits);
3. The agreement extended beyond allegedly infringing products to all terazosin products;
4. The agreement prohibited Geneva from transferring or relinquishing the 180-day exclusivity period; and
5. Finally, "and perhaps most importantly," there was no judicial review of the agreement.

Subsequently and consistently with Commissioner Anthony's remarks, Commissioner Leary, in a speech concerning settlements between NDA holders and ANDA filers,⁶⁸ distinguished reverse payments in consideration for delayed generic launch from stipulated preliminary injunctions on the following grounds:

1. Reverse payments are not refundable;
2. Reverse payments may exceed the ANDA filer's projected lost profits;
3. Reverse payments, in some cases, are made in the context of a stipulated dismissal of litigation.

Again, these distinctions may be more suitable for the forward-looking rule that the two Commissioners had before them, because the remedy in both cases was a cease-and-desist order. One can well imagine, for example, situations in which the parties might have thought it rational to make payments that are not contingent on success in the patent litigation by the generic firm and in excess of the generic firm's expected lost profits. Suppose, for example, that the alleged infringer has only a 30 percent chance of proving that the patent is invalid or not infringed. Suppose that if it enters the market, it will earn \$100 million. The patentee would of course lose much more than that, because the patentee is charging a higher price for the volume it loses than the generic will charge for the volume it gains, because the generic must be sold at a discount to the pioneer product. Therefore, suppose that the patentee would lose \$400 million if the alleged infringer enters. One would think that the generic firm would not enter the

market in such a situation, because it could be liable in damages for \$400 million, with judicial discretion to treble the damages if the court finds willful infringement. Suppose further that the generic firm is in financial trouble and desperately needs a product. If it gets desperate enough, it may enter even if it thinks it should lose the patent litigation. If by a stroke of luck it happens to win, it will make millions. If it loses, it will be judgment proof. The pioneer company might be entitled to hundreds of millions, but how will it ever collect? A mere bond in the event the generic firm ultimately succeeds in the litigation might not be sufficient to forestall entry, because the generic firm may feel it cannot wait that long. One could well imagine a bargain being struck for interim payments in such a circumstance.

The FTC's Generic Drug Study

As already noted, the FTC undertook a year-long study of generic entry under the HWA. One part of its final report, issued in July 2002, analyzes 20 final and 4 interim patent infringement settlement agreements between pharmaceutical companies and first ANDA filers between 1992 and 2000 and makes legislative recommendations concerning such agreements.

The legislative recommendations, with respect to patent settlements are: (1) to require pioneer pharmaceutical companies and first generic entrants to file copies of certain agreements with the FTC and Department of Justice; (2) that the HWA's reference to "commercial marketing" as the triggering event of the 180-day period be defined to include any marketing activity by the first generic entrant, including the entry into a supply agreement with a pioneer manufacturer for the latter to supply drug products to the applicant; (3) that the Act's reference to "court decision," which can trigger the running of the 180-day period, be interpreted as the decision of *any* court on the same patent being litigated by the first applicant, and (4) that the definition of such a "court decision" include any court decision dismissing a declaratory judgment action for lack of a case or controversy.

Among the findings in the report are that 14 of the 20 final agreements had the potential to delay the start of the first ANDA filer's 180 day exclusivity period.⁶⁹ Nine of the final agreements involved the making of "reverse payments" by the pharmaceutical company to the generic drug manufacturer.⁷⁰ In seven of the final agreements, the pioneer pharmaceutical companies granted licenses to the first ANDA filers to permit them to market their generic products prior to patent expiration. In two of the final agreements, the pioneer pharmaceutical companies permitted the ANDA filers to market generic products under the original NDAs rather than under the ANDA filers' own ANDAs.

Perhaps the most noteworthy finding, however, is that since April 1999, when FTC investigations in this area first became public, not a single agreement of the kind challenged by the FTC has been entered. The powerful deterrent effect of FTC action in this area calls into question whether legislation of the kind recommended by the FTC is needed, and raises the possibility that there has been over deterrence of socially beneficial settlements.

Conclusions

Whether or not the HWA is sufficiently favorable to generic drug manufacturers to satisfy the public's need for low cost drugs or too favorable, such that the incentive to invest in the discovery and development of new drugs is dangerously diminished, is open to debate. What cannot be debated is that the HWA has had the intended effect of encouraging the development and marketing of generic versions of pioneer drugs to a significant extent. Also, while the HWA may have opened a Pandora's Box of creative and, in some cases, aggressive product lifecycle management strategies, which in turn have resulted in numerous disputes and litigations, most ANDA applications are approved without patent disputes.⁷¹ Furthermore, while there remain uncertainties about how the HWA should be implemented and how various provisions of the HWA comport with the antitrust laws, it appears unlikely that pioneer pharmaceutical companies will engage in egregious behavior in view of the FTC enforcement actions and the numerous private civil actions.

As pharmaceutical product lifecycle management strategies evolve, it is likely that they will depend more and more heavily on product innovations that drive prescribers towards improved, patent-protected products, which improvements, happily, will benefit patients. As is apparent from this discussion, product innovation strategies are most likely to be immune from antitrust liability. Nevertheless, such strategies will continue to come under close scrutiny and will require careful antitrust analysis to guard against possible liability for monopolization, unlawful conspiracies in restraint of trade, and unfair trade practices.

In spite of the FTC enforcement actions and related civil actions, patent enforcement and settlement will necessarily continue to be integral to pharmaceutical product lifecycle management strategies. Settlement agreements are likely to provoke the closest scrutiny by competitors, the FTC, state attorneys general, insurers, consumer groups, and other affected parties, especially if they contain a "red flag," *e.g.*, reverse payments, absence of judicial review, and ancillary restraints. In any case, parties seeking to settle patent infringement litigations, especially on terms that reflect a business solution, *i.e.*, that do not effectively

produce a total victory for one side or the other, must tread cautiously.

Recent FTC Complaint and Consent Order

The FTC recently proposed a Consent Order with BMS⁷² in an action relating to Taxol, Platinol, and BuSpar.⁷³ In each case, BMS listed new patents in the Orange Book after ANDAs had been filed. Under the HWA, the ANDA filers had to submit new paragraph iv certifications concerning the late-listed patents, after which BMS sued the ANDA filers for infringement, thus triggering new 30-month stays of ANDA approval. The FTC alleged that BMS listed the patents, without a good faith belief that they were valid and met the criteria for listing, in order to trigger improper 30-month stays.

The FTC also alleged that BMS entered into two improper settlement agreements. In one, BMS allegedly paid a generic manufacturer of BuSpar, Schein, to stay off the market until expiration of the original patent. In the other, BMS allegedly conspired with a generic manufacturer, ABI, to license an invalid patent and to list it in the Orange Book as covering Taxol.

Under the Proposed Consent Order, BMS agreed that it:

1. Would relinquish the right to obtain an automatic 30-month stay for any infringement suit based on a patent that was listed in the Orange Book after an ANDA was filed.
2. Would relinquish the right to the automatic 30-month stay regardless of when the patent was listed if BMS: (a) engaged in inequitable conduct

before the PTO in obtaining the patent; (b) made false or misleading statements to the FDA in listing the patent; or (c) provided information to the FDA that is inconsistent with information provided to the PTO.

3. Would not settle any patent infringement claim (including those settled without litigation) through any agreement whereby BMS would make reverse payments or otherwise transfer something of value to the ANDA filer and the ANDA filer would agree not to market its product for some period of time.
4. Would not agree with any ANDA filer that the ANDA filer will not develop or market a generic drug that is not subject to an infringement claim.
5. Would not participate in the enforcement or licensing of a patent with respect to an ANDA filer for any patent to which BMS acquires a nonexclusive license after an ANDA has been filed.⁷⁴

Although BMS waived the right to 30-month stays for late-listed patents, it may sue a generic manufacturer for infringing such patents and may seek preliminary injunctions.

Remarkably, the counts concerning the settlements lack allegations regarding the effects of the agreements on competition in a relevant market. This apparently reflects the FTC staff's position that such agreements should be condemned without a full rule of reason inquiry, despite the ALJ's contrary finding in the Schering-Plough matter.⁷⁵

The proposed Consent Order against BMS highlights the care that must be taken in listing patents in the Orange Book and in entering into patent litigation settlements.

1. Complaint, In the Matter of Hoechst Marion Roussel, Inc., et al. (No. 9293) (Mar. 16, 2000), <http://www.ftc.gov/os/2000/03/hoechstandrxcomplaint.htm>.
2. See discussion of Biovail Corporation Int'l v. Hoechst A.G., *infra*.
3. See Decision and Order, In the Matter of Hoechst Marion Roussel, Inc., et al. (No. 9293) (Apr. 2, 2001), <http://www.ftc.gov/os/2001/04/hoechstdo.pdf>.
4. Although not mentioned in the complaint, Geneva also settled a patent infringement action against Zenith Goldline Pharmaceuticals Inc. (Zenith), which had filed an ANDA for terazosin HCl after Geneva's ANDA was filed, on terms that included that Abbott and Zenith would jointly move to dismiss the patent litigation and Zenith would refrain from marketing its generic in exchange for monetary payments by Abbott to Zenith.
5. See Complaint, In the Matter of Abbott Labs. and Geneva Pharm., Inc. (No. C-3945) (May 2000), <http://www.ftc.gov/os/2000/05/c3945complaint.htm>. Links to the Decision and Order and the statement of the commissioners may be found at <http://www.ftc.gov/os/2000/05/index.htm#26>.
6. Interestingly, the complaint quoted remarks concerning the settlement by Geneva's CEO, stating:
In the words of Geneva's CEO at the time the Agreement was signed, this Agreement represented to Geneva the "best of all worlds," because Geneva obtained a risk-free "monetary settlement on an ongoing basis until the litigation was resolved" and still could market its product exclusively for 180 days after the litigation was over. *Id.*
7. See Decision and Order, In the Matter of Abbott Labs. (No. C-3945) (May 22, 2000), <http://www.ftc.gov/os/2000/05/c3945do.htm>.
8. See Complaint, In the Matter of Schering-Plough Corp., et al. (No. 9297) (Mar. 30, 2001), <http://www.ftc.gov/os/2001/04/scheringpart3comp.pdf>.
9. See Consent Agreement, In the Matter of Schering-Plough Corp., et al. (No. 9297) (Oct. 9, 2001), <http://www.ftc.gov/os/2002/02/ahpagree.pdf>.
10. Actually, in the Cardizem matter, the agreement provided for a license whereby the generic firm could enter prior to patent expiration. See Complaint ¶ 23, In re Hoechst Marion Roussel, Inc. (No. 9293) (Mar. 16, 2000).

11. In addition to these administrative actions, there have been reports of several other FTC investigations, including reports of investigations of settlements between Barr and AstraZeneca concerning Nolvadex® tamoxifen, between Barr and Bayer concerning Cipro® ciprofloxacin, and between BMS and Schein Pharmaceuticals Inc. (Schein) concerning BuSpar.
In the tamoxifen settlement, Barr and Zeneca (now AstraZeneca) settled their patent infringement litigation, including by entering into a nonexclusive supply and distribution agreement under which Barr purchases tamoxifen directly from the innovator, Zeneca, and sells it as a generic product. Barr also has its own ANDA for the manufacture of tamoxifen and, at the time of patent expiration in August 2002 (or should another company's patent challenge succeed), Barr will immediately be permitted to begin the direct manufacture of tamoxifen. See *The Philadelphia Inquirer*, January 1, 1999.
In the ciprofloxacin settlement, Barr and Bayer reached an agreement similar to the tamoxifen settlement agreement except that in this case, Bayer had the option of selling ciprofloxacin to Barr for sale by Barr as a generic or to make payments to Barr and, in any event, Barr was permitted to enter the market 6 months prior to patent expiration. See Barr Press Release, January 17, 1997, <http://www.barrlabs.com/pages/nprpr.html>.
In the buspirone settlement, entered into in December 1994, BMS agreed to make monetary payments to Schein in exchange for which Schein agreed not to market generic buspirone. See *In re Buspirone Antitrust Litig.*, 185 F. Supp. 2d 363 (S.D.N.Y. 2002).
12. See *Mova Pharms. Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998).
13. See discussion of *Andrx v. Friedmann et al.*, Civil Action 98-0099 (D.D.C. Jan. 6, 2000), *infra*.
14. *Andrx v. Friedman*, 83 F. Supp. 2d 179 (D.D.C. 2000).
15. *Id.* at 184.
16. *Id.* at 183 n.5.
17. 256 F.3d at 807.
18. The situation is even more complicated than this summary indicates. Not described here, for example, are patent battles with Mylan and Faulding, a Citizen

- Petition filed with FDA by Andrx requesting the FDA not to approve Biovail's ANDA on the ground that the pK profile of Biovail's generic differs from that of the pioneer product, and political lobbying, in addition to several consumer class actions alleging antitrust law violations.
19. 49 F. Supp. 2d at 767.
 20. *Id.* at 768.
 21. *Zeneca v. Pharmachemie B.V.*, 37 F. Supp. 2d 85 (D. Mass. 1999).
 22. *See Imperial Chem. Indus., PLC v. Barr Labs., Inc.*, 795 F. Supp. 619 (S.D.N.Y. 1992).
 23. *Zeneca* at 93.
 24. *Id.*
 25. *See In re Cardizem CD Antitrust Litig.*, 105 F. Supp 2d 682 (E.D. Mich. 2000).
 26. *Id.* at 618.
 27. *McGuire Oil Co. v. Mapco, Inc.*, 958 F.2d 1552, 1560 (11th Cir. 1992).
 28. *Duplan Corp. v. Deering Milliken, Inc.*, 444 F. Supp. 648, 683 (D. S.C. 1979), *rev'd in part on other grounds*, 594 F.2d 979 (4th Cir. 1979).
 29. *Professional Real Est. Investors, Inc. v. Columbia Pictures Indus., Inc.*, 508 U.S. 49, 113 S. Ct. 1920 (1993).
 30. 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications, 64 Fed. Reg. 42873, 42874-75 (Aug. 6, 1999) (to be codified at 21 C.F.R. pt. 314).
 31. *See In re Terazosin Hydrochloride Antitrust Litig.*, 164 F. Supp 2d 1340 (S.D. Fla. 2000).
 32. *Id.* at 1348-1349.
 33. *United States v. Realty Multi-List, Inc.*, 629 F.2d 1351, 1364 (5th Cir. 1980).
 34. *Terazosin* at 1349 (citing *United States v. Topco Assocs., Inc.*, 405 U.S. 596, 608 (1972)).
 35. Abbott's request for an interlocutory appeal was supported by an *amicus* brief filed by one of the authors (S.P. Mahinka) on behalf of the Washington Legal Foundation.
 36. *See In re K-Dur Antitrust Litig.*, 162 F. Supp. 2d 688 (August 2001).
 37. *See* <http://www.prescriptionaccesslitigation.org/currentcases.htm>.
 38. "NYC PBA Files Federal Class-Action Lawsuits Charging Pharmaceutical Companies With Illegally Inflating Prescription Drug Prices," *PR Newswire*, Aug. 21, 2001.
 39. *See In re Buspirone Antitrust Litig.*, MDL Docket No. 1410, Opinion and Order No. 19 (S.D.N.Y. Feb. 14, 2002). *See also* http://www.prescriptionaccesslitigation.org/html/april_01.html.
 40. All plaintiffs additionally asserted that BMS' conduct in listing the "metabolite patent" in the Orange Book and subsequently suing under that patent violated Section 2 of the Sherman Act. With respect to these allegations, the Court refused to dismiss the complaints on the basis of BMS' assertion that the listing was protected by Noerr-Pennington because (1) listing a patent is not akin to petitioning the government because the FDA lists all submitted patent information without exercise of judgment and, even more interestingly, (2) the listing by BMS was fraud on the FDA and therefore was not protected by Noerr-Pennington under Walker Process *Inc. v. Food Machinery and Chem. Corp.*, 382 U.S. 172, 86 S. Ct. 347 (1966) and, (3) in any event, the activities, as pleaded, failed the two-part (objective and subjective) test of *Professional Real Est. Investors, Inc. v. Columbia Pictures Indus., Inc.*, 508 U.S. 49, 113 S. Ct. 1920 (1993). This issue is discussed *supra*.
 41. 15 U.S.C. § 15b (1994).
 42. "Florida Joins In Antitrust Drug Lawsuit," *The Associated Press*, Sept. 27, 2001.
 43. "State AG Sues Trio of Drug Firms Over Drug," *The Denver Post*, Sept. 28, 2001.
 44. "Barr/AstraZeneca Tamoxifen Settlement Under Investigation by State AGs," *F-D-C Reports* (The Pink Sheet) (Sept. 3, 2001); "Barr's Entitlement to Tamoxifen Exclusivity Questioned," *Marketletter* (Sept. 3, 2001).
 45. Barr Press Release, December 18, 2001, <http://www.barrlabs.com/pages/nrpr.html>.
 46. *See* <http://www.prescriptionaccesslitigation.org/index.htm>. *See also* PBA Press Release, August 21, 2001, <http://www.rycpba.org/releases/pr010821.html>.
 47. PBA Press Release, August 21, 2001, <http://www.rycpba.org/releases/pr010821.html>.
 48. *Id.*
 49. *See* <http://www.prescriptionaccesslitigation.org/index.htm>.
 50. Department of Justice and Federal Trade Commission, Antitrust Guidelines for the Licensing of Intellectual Property (April 6, 1995).
 51. *Id.* at 6 (Example 1).
 52. *Id.* at *23-26, citing *Topco Assocs., Inc.*, 405 U.S. 596, 608 (1972).
 53. Art. I, sec. 8, para. 8.
 54. *See, e.g.*, Frank H. Easterbrook, "Ignorance and Antitrust," in *Antitrust, Innovation, & Competitiveness* 82 (Thomas M. Jorde & David J. Teece eds., 1992), at 122-123: An antitrust policy that reduced prices by 5 percent today at the expense of reducing by 1 percent the annual rate at which innovation lowers the costs of production would be a calamity. In the long run a continuous rate of change, compounded, swamps static losses.
 55. ABA Section of Antitrust Law, Antitrust Law Developments 160 (5th ed. 2003).
 56. *Id.*
 57. *See, e.g.*, Willard K. Torn, "The 1975 Xerox Consent Decree: Ancient Artifacts and Current Tensions," 68 *Antitrust L.J.* 967 (2001); Willard K. Torn & Joshua A. Newberg, "Antitrust and Intellectual Property: From Separate Spheres to Unified Field," 66 *Antitrust L.J.* 167 (1997).
 58. Complaint, In the Matter of Summit Technology, Inc. and VISX, Inc. (No. 9286) (Mar. 24, 1998), <http://www.ftc.gov/os/1998/9803/summit.cmp.htm>.
 59. That is not to say that Summit-VISX was a bad case or should not have been brought. The short term benefits for consumers were substantial, and for current purposes we can only take at face value the FTC's assertion that the two firms would have competed absent a license. Moreover, it is clear from the Analysis to Aid Public Comment that the Commission, did, in fact, weigh considerations such as the efficiencies of settlement in deciding whether to bring the case. Analysis of Proposed Consent Order to Aid Public Comment, In the Matter of Summit Technology, Inc. and VISX, Inc. (No. 9286) (Aug. 21, 1998), <http://www.ftc.gov/os/1998/9808/d09286ana.htm>. As a general approach to patent settlement cases, however, a framework in which the Commission first determines whether there would likely have been lawful horizontal competition absent a license, then applies a *per se* rule, is likely to be a troublesome one.
 60. Thomas B. Leary, "Antitrust Issues in the Settlement of Pharmaceutical Patent Disputes, Part II," presented to American Bar Association Antitrust Healthcare Program (May 10, 2001), <http://www.ftc.gov/speeches/leary/learypharmaceuticalsettlement.htm>.
 61. Barr also settled litigation regarding Ortho-McNeil Pharmaceutical, Inc.'s patents protecting Ortho-Novum 7/77(R) oral contraceptive. According to a Barr press release issued October 29, 2001, as a result of the settlement, Barr will be permitted to introduce a generic product under a nonexclusive license nine months prior to the expiration of the Ortho-Novum 7/77 patents. As part of the settlement, Barr acknowledged its infringement of, and the validity and enforceability of, the patent claims at issue in the case. Barr also stated that the settlement of the Ortho-Novum 7/77 litigation did not affect Barr's challenge of the patents protecting another of Ortho-McNeil's oral contraceptive products. *See* <http://www.barrlabs.com/pages/nrpr.html>.
 62. Barr Press Release, April 2, 2001, <http://www.barrlabs.com/pages/nrpr.html>.
 63. Barr Press Release, May 9, 2001, <http://www.barrlabs.com/pages/nrpr.html>.
 64. Sheila F. Anthony, "Riddles and Lessons from the Prescription Drug Wars: Antitrust Implications of Certain Types of Agreements Involving Intellectual Property," presented to American Bar Association Antitrust and Intellectual Property Crossroads Program (June 1, 2000), <http://www.ftc.gov/speeches/anthony/sfp000601.htm>.
 65. The forward-looking nature of § 5 has been noted in III Phillip E. Areeda & Herbert Hovenkamp, *Antitrust Law* ¶ 651d at 79 (rev. ed. 1997) (hereinafter *Areeda & Hovenkamp*) ("The FTC Act was clearly conceived as a supplement to the Sherman Act, a vehicle for evolving, through administrative expertise, prohibitions of conduct not formerly thought unlawful or contrary to good business morals."). *See also* II *Areeda & Hovenkamp* ¶ 307c at 25 (rev. ed. 1995) ("The Commission should feel free to 'enjoin' any unjustified behavior that tends to impair competition and is capable of being differentiated adequately from permissible behavior").
 66. 35 U.S.C. § 271(e)(2) (1994).
 67. Sheila F. Anthony, *supra* n.64.
 68. Thomas B. Leary, *supra* n.60.
 69. Federal Trade Commission, Generic Drug Entry Prior to Patent Expiration: An FTC Study (July 2002), at 25, <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>.
 70. *Id.*
 71. According to statistics published by the Pharmaceutical Research and Manufacturers Association of America, of the 8,259 ANDA applications filed from 1984 through January 2001, 94 percent, or 7,784 applications, did not raise patent issues. *See* <http://www.phrma.org/publications/documents/backgrounders/2002-04-22.399.html>.
 72. *See* Complaint, In the Matter of Bristol-Myers Squibb Co., (File Nos. 001 0221, 011 0046, and 021 0181) (March 7, 2003), <http://www.ftc.gov/os/2003/03/bristolmyerscmp.pdf>.
 73. BMS already agreed to pay \$670 million to settle private antitrust litigation relating to BuSpar and Taxol. *See* F-D-C Reports (Pink Sheet) at 24 (Jan. 13, 2003).
 74. Decision and Order, ¶¶ VII, XI, XII, In the Matter of Bristol-Myers Squibb Co., (File Nos. 001 0221, 011 0046, and 021 0181) (March 7, 2003), <http://www.ftc.gov/os/2003/03/bristolmyersdo.pdf>. The "reverse payments" provision has two exceptions: (1) when the value provided to the ANDA filer is no more than the right to market the ANDA product prior to the expiration of the patent and BMS' expected litigation costs to resolve the infringement claim (which are capped at \$2 million) and (2) if BMS obtains an advisory opinion from the FTC that the settlement would not raise issues under Section 5 of the FTC Act.
 75. An FTC staff attorney referred to any settlement of late-listed patent litigation that includes a reverse payment as "highly suspect," apparently without regard to the validity of the patent. *See* "FTC Says Bristol-Myers Squibb Abused Government Process to Stifle Generic Competition," *FTC Watch* at 12 (March 17, 2003).