
Licensing Markets

The *Licensing Journal* is privileged to welcome Ernest V. Linek to its board of columnists, whose section devoted to Biotechnology and Pharmaceutical Licensing matters debuts in this month's issue. In over 25 years of practice, Ernest Linek has successfully prosecuted hundreds of US and international patent applications in fields including natural product chemistry, polymer chemistry, pharmaceuticals, biotechnology, electroplating, semiconductors, and photoreceptors. He also is very active in providing client counseling and opinions regarding the validity and infringement of patents and trademarks. Mr. Linek has extensive litigation experience and has successfully protected his client's interests in numerous Federal District Courts and before the US Court of Appeals for the Federal Circuit. Mr. Linek was selected to appear on the 2007 New England Super Lawyers list by the publishers of *Law and Politics Magazine*.



Biotechnology and Pharmaceutical Licensing

Ernest V. Linek

This column is intended to provide suggestions and case commentary that may assist the reader in dealing with licensing issues in technological areas where the Federal Food and Drug Administration (FDA) has jurisdiction over your ultimate products, namely, the fields of biotechnology, pharmaceuticals, and medical devices.

Future columns will address issues and aspects regarding the licensing-in and/or the licensing-out of new drugs and medical devices. Topics will include licensing issues that may arise during the development phase, preclinical phase, and clinical phases of drugs and medical devices. I welcome your emails regarding suggested future topics for the column.

This column begins at the end of the drug development process: The

FDA has approved the marketing of a new drug; one or more patents regarding the drug have been granted by the USPTO; and one or more generic drug manufacturers are interested in obtaining FDA permission to sell a generic version of the drug.

The commercial impact of generic drugs is staggering. When a generic version of any drug hits the market, the price for that drug falls, often by as much as 80 to 90 percent.

The Hatch-Waxman Act governs the FDA's approval of new and generic drugs. The goal of this act is to strike a balance between two competing policy interests: (1) inducing pioneering research and development of new drugs and (2) enabling competitors to bring low-cost, generic copies of

those drugs to market as soon as possible.

First, the pioneering drug company must obtain FDA approval for its drug by submitting a New Drug Application (NDA). As part of the NDA process, the drug company must inform the FDA of all patents covering its drug or the methods of using the drug. The identified patents are those on which a claim of patent infringement could reasonably be asserted, if a person was not licensed by the patent owner, for the manufacture, use, or sale of the drug. The FDA lists all such patents in a publication titled the "Approved Drug Products with Therapeutic Equivalence Evaluations." Because of the color of the cover of this publication, it is commonly known as the "Orange Book." Drugs approved by the FDA are known as "listed drugs."

Second, to facilitate the development of generic versions of listed drugs, the Hatch-Waxman Act provides the Abbreviated New Drug Application (ANDA) process for generic drug manufacturers. The ANDA process streamlines FDA approval of generic drugs by allowing these applicants to rely on the results of the safety and efficacy studies that supported the FDA's original approval of a listed drug.

Under the ANDA process, a generic drug company must submit information to show that the generic drug and the relevant listed drug share the same active ingredients and are bioequivalent. In addition, generic drug companies must submit one of four certifications addressing each Orange Book listed patent covering the listed drug, namely:

1. That the required patent information has not been filed with the FDA; or

2. That all such patents have expired; or
3. The date on which all such patents will expire; or
4. That all such patents are invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the ANDA is submitted.

Thus, the Hatch-Waxman Act provides that if a generic drug company wants to market a generic version of a listed drug before the expiration of all Orange Book listed patents covering that drug, it must file a Paragraph IV Certification—stating that the patents are either invalid or not infringed (or both).

All Paragraph IV ANDA filers must provide notice of their Paragraph IV Certification to both the patent owner and the NDA holder. This notice must set forth a detailed statement of the factual and legal basis for the opinion of the ANDA applicant that the patent is invalid or will not be infringed.

Third, the Hatch-Waxman Act facilitates the early resolution of patent disputes between generic and pioneering drug companies by providing that the mere act of filing an ANDA based on a Paragraph IV Certification constitutes an act of patent infringement. Under Hatch-Waxman, the act of filing a patent infringement suit against an ANDA filer triggers a 30-month stay that prohibits generic entry.

Fourth, as an incentive for ANDA filers to challenge the validity of listed patents or to design around those patents as early as possible, the Hatch-Waxman Act provides that the first ANDA applicant to file a Paragraph IV Certification (first Paragraph IV ANDA filer) shall enjoy a 180-day period of generic marketing exclusivity.

Market exclusivity, even for only 180-days, can be very important in the success of a generic drug launch.

Until the first Paragraph IV ANDA filer's exclusivity period expires, the FDA may not approve a later-filed Paragraph IV ANDA based on the same NDA (hereinafter a subsequent Paragraph IV ANDA).

More importantly, the first Paragraph IV ANDA filer is entitled to the 180-day exclusivity period whether or not it establishes that the NDA holder's Orange Book listed patents are invalid or not infringed by the drug described in its ANDA. All that is required is that the first Paragraph IV ANDA filer submits a substantially complete ANDA that contains a Paragraph IV Certification.

The Hatch-Waxman Act provides that the 180-day period of exclusivity begins either on the date that the first Paragraph IV ANDA filer begins marketing its generic drug, or on the date of a final court decision finding the relevant Orange-Book-listed patents invalid or not infringed, whichever comes first.

In other words, the applicable statutory provisions provide for two methods of triggering the first Paragraph IV ANDA filer's 180-day exclusivity period:

- A commercial marketing trigger; and
- A court-judgment trigger
- Only the first Paragraph IV ANDA filer can trigger its 180-day exclusivity period via the commercial marketing trigger. However, any subsequent Paragraph IV ANDA filer can trigger the first Paragraph IV ANDA filer's 180-day exclusivity period via the court-judgment trigger.

- Because the FDA cannot approve any subsequent Paragraph IV ANDA until the first Paragraph IV ANDA filer's 180-day exclusivity period expires, the date on which the exclusivity period is triggered is critical to both NDA holders and subsequent Paragraph IV ANDA filers.

With this background, let's now look at some recent cases related to this area.

ANDA Filer Can Bring a Declaratory Judgment Action against Listed Drug Patents

In *Caraco Pharmaceutical Laboratories, Ltd. v. Forest Laboratories, Inc.*, the Court of Appeals for the Federal Circuit (CAFC) held that Caraco, a second ANDA filer, could maintain a declaratory judgment action seeking to invalidate an Orange Book Listed Patent, even though the patentee had unilaterally granted Caraco an irrevocable covenant not to sue for infringement of the patent. Forest's stated goal in granting the covenant to Caraco was to confirm that there was no case or controversy between the parties regarding the patent.

The CAFC, following the Supreme Court's 2007 decision in *Medimmune, Inc. v. Genentech, Inc.*, reviewed the controversy using the three-part framework for determining whether the DJ action presented a justiciable Article III controversy. An action is justiciable under Article III only if: (1) the plaintiff has standing, (2) the issues presented are ripe for judicial review, and (3) the case is not rendered moot at any stage of the litigation. Based

on these factors, the CAFC held that, regardless of the covenant not to sue, Caraco's DJ action satisfies these requirements and presents a justiciable Article III controversy.

Forest holds an approved NDA for its drug Lexapro®, which is used to treat depression and generalized anxiety disorder. As part of its NDA, Forest listed two patents in the FDA's Orange Book: the '712 patent the '941 patent.

The first ANDA applicant to file a Paragraph IV Certification for Forest's '712 and '941 patents was Ivax Pharmaceuticals, Inc. Thus, Ivax is entitled to 180 days of generic market exclusivity, which will begin either on the day it begins marketing its generic drug, or on the date a court determines that the '712 and '941 patents are invalid or not infringed—whichever comes first.

Forest responded to Ivax's Paragraph IV ANDA by suing Ivax for infringement of the '712 patent, the earlier of the two patents to expire. Ivax counterclaimed that the '712 patent was invalid. Forest did not sue Ivax for infringement of the '941 patent.

Ultimately, Forest defeated Ivax's counterclaim of invalidity of the '712 patent and obtained a district court judgment that the drug described in Ivax's ANDA infringed the '712 patent, which was affirmed by this CAFC.

Because Ivax did not obtain a judgment that both of Forest's Orange Book listed patents were invalid or not infringed by the generic drug described in its ANDA, Ivax failed to trigger its 180-day exclusivity period via the court-judgment trigger.

In addition, because the generic drug described in Ivax's ANDA was found to infringe the '712

patent, Ivax cannot trigger its 180-day exclusivity period via the commercial-marketing trigger. Indeed, the district court specifically enjoined Ivax from making, using, offering to sell or selling within the United States, or importing into the United States any products that infringe the '712 patent, including the drug products referred to in Ivax's ANDA until such time as the '712 patent expires.

In 2006, Caraco filed an ANDA for generic drug that included a Paragraph IV Certification for Forest's '712 and '941 patents for Lexapro®. Forest sued Caraco for infringement of the '712 patent. As in the *Ivax* case, Forest did not sue on the '941 patent.

However as discussed above, under the Hatch-Waxman Act, Caraco has an economic interest in determining whether the '941 patent is invalid or not infringed by the drug described in its ANDA, because only a judgment of invalidity or noninfringement with respect to both the '712 and '941 patents can trigger Ivax's 180 day exclusivity period. On day 181 Caraco would then be free to sell its generic version of the drug. Thus, Caraco filed a separate Declaratory Judgment action seeking judgment that the drug described in its ANDA does not infringe Forest's '941 patent.

Forest filed a motion to dismiss Caraco's DJ action on the grounds that the action did not present a "case" or "controversy" as required by Article III of the Constitution. The district court granted Forest's motion and Caraco appealed to the CAFC, which, following *Medimmune*, reversed.

ANDA Settlements

In April 2008 AstraZeneca settled a patent infringement case

with Ranbaxy Laboratories over its Nexium ulcer drug. Ranbaxy had filed an ANDA to market a generic version of the drug. Under the settlement, Ranbaxy will wait until May 2014 before producing its generic version of the drug (an "authorized generic") under license from AstraZeneca. The 2014 date marks the expiration of two of AstraZeneca's six patents on the drug. The other patents expire between 2014 and 2019.

These cases often are settled by a license agreement between the patent owner first drug company granting a license to the generic drug company, so that the drug sold by them becomes an "authorized generic." Such settlements/licenses are reviewed by the FTC for anticompetitive effects.

FTC Review of Settlements

In February 2008 the Federal Trade Commission (FTC) filed suit against Cephalon Inc. and its settlements with four generic firms regarding the company's drug Provigil. The FTC alleges that these settlements, and, in particular, the payments from Cephalon to the generic firms accompanying each of these settlements, was anticompetitive, as it caused the generic firms to delay their entry into the market until 2012.

The facts surrounding the Cephalon case present several interesting issues, namely:

- The case was brought against the brand firm on monopolization grounds under Sherman Act Section 2. Previously, the FTC had based generic settlement challenges under Sherman Act Section 1.
- The FTC filed suit in the District of Columbia district

court, rather than bringing the case through its own administrative trial process.

- The 27 page Complaint provides significant detail on the manner in which the alleged

payments were made by Cephalon to the generic firms. The allegations regarding these inducements provide guidance on the types of circumstances under which the FTC might

investigate or challenge such deals in the future.

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