180-day exclusivity is hotly contested

Recent cases addressed how provision can be invoked and triggered.

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IN 1984, CONGRESS enacted the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984), commonly known by the names of its principal sponsors as the Hatch-Waxman Act. The act provides the legislative foundation for the generic drug approval process and the protection of pharmaceutical patent rights, and establishes a framework for both competition and innovation within the pharmaceutical industry. One provision of this act, the “180-day exclusivity” provision, has been a source of significant controversy as well as a great deal of recent activity in the Food and Drug Administration (FDA) and the courts.

The Hatch-Waxman Act consists of a number of amendments to the federal drug and patent laws. The amendments streamline the approval requirements for generic drugs as part of a package of substantive and procedural rights intended to safeguard pharmaceutical patents and maintain incentives for innovation. Among other things, the act provides procedures for identifying relevant patents and resolving infringement issues before FDA approval of a proposed generic product. The 180-day exclusivity provision, codified at 21 U.S.C. 355(j)(5)(B)(iv), benefits generic companies by providing 180 days of marketing exclusivity to the first filer of an abbreviated new drug application (ANDA), the basis for approval of generic drugs, which challenges the validity, enforceability or infringement of a patent “listed” in connection with a pioneer drug.

This challenge is made in the ANDA through a Paragraph IV certification, by which an ANDA filer states its position that a particular patent is invalid, unenforceable or not infringed. Under federal patent law, submitting an ANDA for a drug protected by patent is itself an act of patent infringement, and its filing enables the pioneer patent holder to litigate any patent infringement issues before FDA approval of the proposed generic product. See 35 U.S.C. 271(e)(2)(A).

The 180-day exclusivity provision then provides the first generic company to file an ANDA containing a Paragraph IV certification with 180 days of marketing exclusivity against competing generics for that same pioneer drug. The FDA is precluded from approving subsequent ANDAs before expiration of the first-filer’s 180-day exclusivity period. The exclusivity period does not begin, however, upon the filing or approval of an ANDA with a Paragraph IV certification. Rather, it is triggered by the earlier of the “first commercial marketing of the drug” or “a decision of a court...holding the patent which is the subject of the certification to be invalid or not infringed.” 21 U.S.C. 355(j)(5)(B)(iv)(I) and (II).

The FDA issued regulations implementing the 180-day exclusivity provision, but these have been invalidated by the courts in important respects. On Aug. 6, 1999, the FDA published proposed regulations that would substantially alter its 180-day exclusivity rules. See 64 Fed. Reg. 42,873. These have not yet been made final. In addition, in March 2000, the FDA issued a “Guidance to Industry,” which sets forth several of the FDA’s current interpretations of the 180-day exclusivity rule.

Invoking exclusivity

Must a first generic successfully defend a patent infringement suit— i.e., establish that the subject patent is invalid or not infringed— in order to be entitled to 180-day exclusivity? The FDA initially said “yes,” until the courts said “no.” This “successful defense” history is illustrative of the uncertainty that surrounds 180-day exclusivity.

Until 1998, FDA regulations required that a first-filer successfully defend a patent infringement suit in order to invoke the 180-day exclusivity period. Thus, an ANDA filer was not entitled to the exclusivity period without successfully defending a patent-infringement suit. In 1997, however, the U.S. District Court for the District of Columbia in Mova Pharm. Corp. v. Shalala, 955 F. Supp. 128 (D.D.C. 1997), struck down this “successful defense” requirement as arbitrary and capricious. The U.S. Court of Appeals for the D.C. Circuit affirmed. Mova Pharm. Corp. v. Shalala, 140 F.3d 1060 (D.C. Cir. 1998).

A later decision made clear that a first generic need not even be sued for patent infringement in the first place. See Purepac Pharm. Co. v. Friedman, 162 F.3d 1201, 1204 (D.C. Cir. 1998). The FDA subsequently issued a guidance document making clear that a successful defense is not required. However, while a successful defense is not required to obtain exclusivity, the loss of a patent infringement case—i.e., a holding that the patent is not invalid or is infringed—will strip the first generic of its rights under the 180-day provision.

Triggering exclusivity

The 180-day exclusivity provision commences upon the earlier of the first commercial marketing of the exclusivity holder’s drug under its ANDA, or a court decision of patent invalidity or noninfringement. The meaning of “court decision” has been evolving. The question has been whether the term refers to the date of a district court decision or whether any appeal must be taken into account. Initially, the FDA took the latter position, holding that the operative date was either the date that a district court decision is affirmed by the Federal Circuit, or the date on which the time for filing an appeal has lapsed.
The D.C. District Court rejected this approach, however, in Mylan Pharm. v. Shalala, 81 F. Supp. 2d 30, 41-2 (D.C. 2000), in which it held that a “decision of a court” means “all court decisions, whether subsequently vacated, settled, appealed or otherwise mooted,” and that the exclusivity period begins on the date of a district court decision finding invalidity, unenforceability or no infringement.

In its March 2000 Guidance to Industry, the FDA abandoned its earlier approach in favor of a district court-based definition of “court decision,” stating that it would apply the new definition only prospectively to ANDAs submitted after publication of the March 2000 Guidance.

It is noteworthy that a triggering court decision need not be in a case involving the first generic; it may be the result of a case between the pioneer and a later ANDA filer. In that circumstance, if a patent is held invalid or not infringed, that decision will trigger commencement of the exclusivity period while the case against the first generic is still pending and before the first generic’s ANDA has been approved by the FDA. This creates the possibility that the first generic’s 180-day exclusivity will expire before it is able to market its product. There has been litigation on this question, but to date courts have upheld the ability of a later ANDA filer to trigger the exclusivity period even when the first generic is unable to market during it. See, e.g., Minnesota Mining and Mfg. Co. (3M) v. Barr Labs., 139 F. Supp. 2d 1109 (D. Minn. 2001).

**Losing exclusivity**

What happens if the patent on which exclusivity is based expires before the commencement of the exclusivity period? The FDA’s position is that exclusivity is lost upon expiration of the patent on which it is based. In a recent example, Dr. Reddy’s Laboratories, a generic manufacturer, lost its exclusivity rights for a particular dose of generic omeprazole when the patent on which it was the first to file expired before the exclusivity period had commenced. As a result, the FDA denied approval of Dr. Reddy’s ANDA pending expiration of the exclusivity period of an ANDA filer that was the first to file on a different patent. See Nov. 16, 2001, Letter from the FDA to Reddy-Cheminor Inc. Dr. Reddy’s recently filed suit against the FDA, challenging the FDA’s interpretation of the statute. See Dr. Reddy’s Labs. v. Thompson, No. 02-CV-452 (D.N.J. filed Jan. 31, 2002).

A first generic can also lose its exclusivity by withdrawing its Paragraph IV certification, which could happen, for example, in connection with a settlement of a patent infringement suit with the pioneer. Withdrawal of a Paragraph IV certification has been held to constitute a forfeiture of the first generic’s 180-day exclusivity rights. See Mylan v. Thompson, No. 01 CV 23, 12001 WL 165478 (N.D. W.Va. April 18, 2001); Mylan Pharm. v. Henney, 94 F. Supp. 2d 36 (D.D.C. 2000), vacated on different grounds as moot, 276 F.3d 627 (D.C. Cir. 2002).

If a first generic does not perfect its rights to 180-day exclusivity for a given patent, will the exclusivity roll over to the next ANDA applicant with a Paragraph IV certification for that patent, i.e., the second to file? The FDA’s current position—set forth in its August 1999 proposed regulations—is that there is no “rolling exclusivity.” The only ANDA applicant eligible for exclusivity is the first one to file a “substantially complete” ANDA containing a Paragraph IV certification, i.e., the first generic. This issue has not been tested in court.

The question of who is entitled to exclusivity can become very complicated when there are multiple patents listed for a pioneer drug and different first generics for the different patents. The FDA’s original approach to this problem, based on its regulations at 21 C.F.R. 314.107, was a “patent-by-patent” approach, in which separate exclusivity periods would be awarded to the various first generics for each listed patent. A recent situation, however, resulted in an “exclusivity stand-off” in which one first generic for a particular patent blocked approval of the ANDA of a different first generic, and vice-versa. The FDA resolved the issue by awarding a single “shared exclusivity” period to the two first generics, which would commence upon the first commercial marketing of either generic product or a court decision on any of the patents on which either product’s claim to exclusivity was based. See Nov. 16, 2001, Letter from the FDA to Andrx Pharmaceuticals Inc., at www.fda.gov/cder/ogd/shared_exclusivity.htm.

In contrast, in the Dr. Reddy’s situation described above, there was no exclusivity stand-off because the patent on which Dr. Reddy’s was the first to file had expired, and Dr. Reddy’s was thus not eligible for exclusivity. Accordingly, the FDA determined that there was no reason for shared exclusivity in that situation. Dr. Reddy’s has challenged various aspects of this decision in federal court.

Another issue is whether different strengths (i.e., dosages) of a drug are eligible for separate 180-day exclusivity periods. The answer is yes. One generic manufacturer can hold a 180-day exclusivity for a 10-milligram dose of a drug, for example, while a different generic manufacturer holds a 180-day exclusivity for a 30-milligram dose. This issue was contested in the mid-1990s but has since been resolved in Apotex v. Shalala, 53 F. Supp. 2d 454 (D.D.C.), aff’d, 1999 WL 956686 (D.C. Cir. 1999). The court noted that permitting separate exclusivity periods for separate drug strengths is consistent with the statute, which requires that an ANDA must contain, among other things, “information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug.” Id. at 456 (quoting 21 U.S.C. 355(j)(2)(A)(iii)). For similar reasons, different forms of the same drug—e.g., tablets and capsules—are also eligible for separate 180-day exclusivity periods.

Finally, the FDA allows a first generic to transfer its 180-day exclusivity rights in certain situations. Pursuant to the FDA’s proposed regulations, a first generic may transfer its exclusivity rights to a specified competitor after the exclusivity period has commenced. See 64 Fed. Reg. 42,873 (Aug. 6, 1999); see also Boehringer Ingelheim Corp. v. Shalala, 993 F. Supp. 1 (D.D.C. 1997) (affirming the FDA’s position). This can be particularly useful to a first generic when its exclusivity has commenced, but it is not yet able to market its product. However, a first generic may not transfer its exclusivity rights before the exclusivity period has begun—i.e., before first commercial marketing or an operative court decision. Of course, it may waive its exclusivity rights entirely at any time, thus allowing the FDA to approve all otherwise eligible ANDAs for that drug.

Congress is currently considering legislation that would modify the 180-day exclusivity provision and make other changes in the Hatch-Waxman Act. The act, however, has generally worked well, and it is not clear that the case for reopening such fundamental legislation has been made.