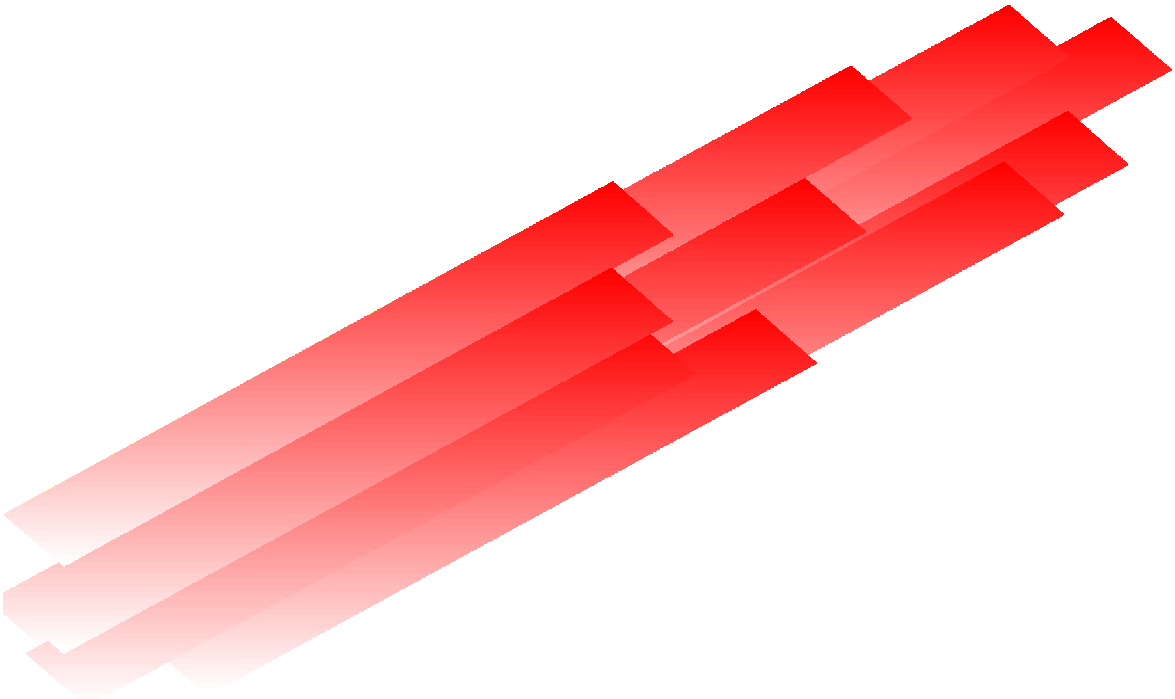
Guidance for Industry

180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act



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Guidance for Industry

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GUIDANCE FOR INDUSTRY[1]

180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act

I. WHY IS FDA ISSUING THIS GUIDANCE?

This guidance is intended to provide industry with information on how the Food and Drug Administration (FDA) is applying the 180-day generic drug exclusivity provisions of the Federal Food, Drug, and Cosmetic Act (the Act) in light of recent court decisions. The guidance addresses the issue of the elimination of the "successful defense" requirement, which required an abbreviated new application (ANDA) applicant to be sued for patent infringement and to prevail in the litigation to receive the 180-day period of marketing exclusivity. This guidance will remain in effect until superseded by new regulations or new guidance.

II. BACKGROUND

The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. No. 98-417) (the Hatch-Waxman Amendments) amended the Federal Food, Drug, and Cosmetic Act (the Act). The Hatch-Waxman Amendments created section 505(j) of the Act (21 U.S.C. 355(j)). Section 505(j) established the abbreviated new drug application (ANDA) approval process, which allows lower-priced generic versions of previously approved innovator drugs to be approved and brought on the market.

Innovator drug applicants must include in a new drug application (NDA) information about patents that claim the drug product that is the subject of the NDA. FDA publishes this patent information as part of the *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is generally known as the *Orange Book*.

An ANDA applicant must include in the ANDA a patent certification described in section 505(j)(2)(A)(vii) of the Act. The certification must make one of the following statements: (I) no patent information on the drug product that is the subject of the ANDA has been submitted to FDA; (II) that such patent has expired; (III) the date on which such patent expires; or (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product

[1] This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. This guidance document represents the Agency's current thinking on section 505(j)(5)(B)(iv) and 180-day generic drug exclusivity. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

for which the ANDA is submitted. This last certification is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA refers. The submission of an ANDA for a drug product that is claimed in a patent is an infringing act if the drug product that is the subject of the ANDA is intended to be marketed before the expiration of the patent and, therefore, may be the basis for patent infringement litigation.

Section 505(j)(5)(B)(iv)[2] of the Act provides an incentive for generic manufacturers to file paragraph IV certifications challenging patents that may be invalid, not infringed by the product that is the subject of the ANDA, or unenforceable, thereby possibly triggering a patent action against them by the patent owner. Section 505(j)(5)(B)(iv) of the Act states that—

> If the [ANDA] contains a [paragraph IV certification] and is for a drug for which a previous application has been submitted under this subsection continuing [sic] such a certification, the application shall be made effective not earlier than one hundred and eighty days after--
>
> > (I) the date the Secretary receives notice from the applicant under the previous [ANDA] of the first commercial marketing of the drug under the previous [ANDA], or
> >
> > (II) the date of a decision of a court in [a patent infringement action] holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

This means that, in certain circumstances, an ANDA applicant whose ANDA contains a paragraph IV certification is protected from competition from subsequent generic versions of the same drug product for 180 days after either the first marketing of the first applicant's drug or a decision of a court holding the patent that is the subject of the paragraph IV certification to be invalid or not infringed.[3] This marketing protection is commonly known as "180-day exclusivity."

In the *Federal Register* of October 3, 1994 (59 FR 50338, 50367), FDA published the final rule implementing the patent and marketing exclusivity provisions of the Hatch-Waxman Amendments. The regulation implementing section 505(j)(5)(B)(iv) of the Act provides:

> If an abbreviated new drug application contains a certification that a relevant

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[2] Prior to the enactment of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act), 180-day exclusivity was described at section 505(j)(4)(B)(iv) of the Act. The Modernization Act added new provisions to section 505(j) that resulted in a renumbering of the sections.

[3] The Agency interprets the term *court* to refer to the court that enters final judgment from which no appeal can be or has been taken (21 CFR 314.107(e)).

> patent is invalid, unenforceable, or will not be infringed and the application is for a generic copy of the same listed drug for which one or more substantially complete abbreviated new drug applications were previously submitted containing a certification that the same patent was invalid, unenforceable, or would not be infringed ***and the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner's receipt of notice submitted under § 314.95***, approval of the subsequent abbreviated new drug application will be made effective no sooner than 180 days from whichever of the following dates is earlier:
>
> > (i) The date the applicant submitting the first application first commences commercial marketing of its drug product; or
> > (ii) The date of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed. (21 CFR 314.107(c)(1)) (emphasis added)

The proposed rule containing § 314.107(c)(1), published in the *Federal Register* of July 10, 1989 (54 FR 28872, 28929), proposed the requirement that the first ANDA applicant submitting a paragraph IV certification be sued for patent infringement to obtain the 180-day exclusivity. This interpretation was believed to be most consistent with the language of the Hatch-Waxman Amendments and furthered the congressional intent to encourage challenges to patents that may be invalid or unenforceable (54 FR 28872 at 28894). In response to a comment on the proposed rule, FDA added a requirement to the final rule that the first ANDA applicant submitting a paragraph IV certification successfully defend a patent infringement suit to be entitled 180-day exclusivity. The "successful defense" requirement was established to eliminate "an incentive for frivolous claims of patent invalidity or noninfringement because it would give ANDA applicants exclusivity even if the applicant was unsuccessful in defending against the patent owner's lawsuit" (59 FR 50338 at 50353).

III. DISCUSSION

FDA's "litigation" and "successful defense" requirements for 180-day exclusivity have been challenged in the courts in *Inwood Laboratories, Inc. v. Young*, 723 F. Supp. 1523 (D.D.C. 1989), *vacated as moot*, 43 Fed. 3d 712 (D.C.Cir. 1989); *Mova Pharmaceutical Corp. v. Shalala*, 955 F. Supp. 128 (D.D.C. 1997), and *Granutec , Inc. v. Shalala*, No. 5:97-CV-485-BO(1) (E.D.N.C. July 3, 1997). The district courts in both *Inwood* and *Mova* held that 180 days of marketing exclusivity should be granted to the first ANDA applicant who files a paragraph IV certification, regardless of whether the applicant is subsequently sued for patent infringement. Following the *Inwood* decision and the initial district court decision in *Mova*, FDA determined that it would be appropriate to acquiesce in the courts' decisions until the issue was resolved by the appellate courts.

The *Mova* decision was upheld in the U.S. Court of Appeals for the District of Columbia Circuit,

Mova Pharmaceutical Corp. v. Shalala. No. 97-5082, 1998 U.S. App. Lexis 7391 (D.C. Cir. Apr. 14, 1998). Following the circuit court decision, on June 1, 1998, the district court in *Mova* entered an order stating that the successful defense requirement of 21 CFR 314.107(c)(1) is invalid and permanently enjoining FDA from enforcing it.

Subsequent to the initial district court decision in *Mova* and FDA's acquiescence, but prior to the Court of Appeals decision, the U.S. District Court for the Eastern District of North Carolina addressed the validity of § 314.107(c)(1) in *Granutec* and, in a holding contrary to the earlier *Mova* district court decision, ordered FDA to follow its regulations in approving ANDAs for ranitidine HCl. The *Granutec* decision was stayed and appealed to the U.S. Court of Appeals for the 4th Circuit, which reversed the district court's decision, *Granutec, Inc. v. Shalala*, No. 97-1873 and No. 97-1874, 1998 U.S. App. LEXIS 6685, (4th Cir. Apr. 3, 1998).

Both the U.S. Court of Appeals for the District of Columbia Circuit and the U.S. Court of Appeals for the 4th Circuit held that FDA's interpretation of section 505(j)(5)(B)(iv) expressed in 21 CFR 314.107(c)(1) is unsupported by the Act. FDA has decided not to appeal either decision. The effect of these decisions, together with the June 1, 1998, order of the district court in *Mova*, is that FDA will not enforce the "successful defense" provisions of § 314.107(c)(1).[4]

FDA intends to formally remove the "successful defense" provisions from § 314.107(c)(1), but that process is not complete. Following withdrawal of the regulatory provision, FDA expects to begin a rulemaking to issue new regulations under section 505(j)(5)(B)(iv). In the meantime, the Agency must make exclusivity decisions for ANDAs that are nearing approval. Until such time as the rulemaking process is complete, FDA will regulate directly from the statute, and will make decisions on 180-day generic drug exclusivity on a case-by-case basis.

This guidance is intended to provide industry with information on how FDA is applying section 505(j)(5)(B)(iv) in light of the decisions in *Mova* and *Granutec*. The Agency will revise this guidance as additional interpretations are made.

IV. WHO IS ELIGIBLE FOR 180-DAY EXCLUSIVITY WHEN THE FIRST APPLICANT TO SUBMIT A SUBSTANTIALLY COMPLETE ANDA WITH A PARAGRAPH IV CERTIFICATION IS NOT SUED?

The first applicant to submit an ANDA with a paragraph IV certification, but who was not sued by the patent owner or NDA sponsor, generally would receive a letter from the Office of Generic Drugs that contains the following information:

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[4] In the *Federal Register* of November 11, 1997 (62 FR 63268), before either court of appeals decision issued, FDA published a clarification stating that the Agency would apply § 314.107(c)(1) as written, including the "successful defense" requirement. In light of subsequent events described in this document, the Agency will not regulate as described in that publication.

At this time we are writing to you to clarify the issue of 180-day exclusivity with respect to your application. In light of the recent court decisions in *Granutec v. Shalala*, and *Mova v. Shalala*, including the district court's order of June 1, 1998, in *Mova* declaring the "successful defense" requirement 21 CFR 314.107(c)(1) invalid and directing FDA not to enforce it, FDA is reinterpreting section 505(j)(5)(B)(iv).

(*Name of applicant*) was the first applicant to submit a substantially complete ANDA with a paragraph IV certification. Although you were not sued as a result of the notice you provided to the holder of the NDA and the patent owner, you are nonetheless eligible for 180 days of market exclusivity. Such exclusivity will begin to run either from the date you begin commercial marketing or from the date of a decision of a court finding the patent invalid or not infringed, whichever is earlier (section 505(j)(5)(B)(iv)). A court decision that can trigger the beginning of exclusivity is a decision of any court in a patent infringement action resulting from a paragraph IV certification in which the court finds that the patent is invalid or not infringed. In a case such as yours, where the first applicant is not sued for patent infringement, the court decision would obviously be rendered in a case involving a subsequent ANDA applicant. With respect to the "first commercial marketing" trigger for the commencement of exclusivity, we draw your attention to 21 CFR 314.107(c)(3) and (4). The Agency expects that you will begin commercial marketing of your product promptly upon approval.

If you have additional questions, please contact Mr. Jerry Phillips, Director, Division of Labeling and Program Support, at 301-827-5846.

An applicant whose final approval would be affected by another's 180-day exclusivity would generally receive a letter containing the same basic information in a different format.

The text of this letter describes the Agency's application of section 505(j)(5)(B)(iv) to the threshold question of whether a ANDA applicant that was not sued for patent infringement as a result of its paragraph IV certification would nonetheless be eligible for exclusivity. There are many additional issues related to the application of the statutory provisions that have yet to be resolved. This guidance will be updated as FDA interprets and applies section 505(j)(5)(B)(iv). As stated above, the Agency intends to undertake a rulemaking to issue new regulations to fully implement the 180-day generic exclusivity provisions in light of recent court decisions.