Guidance for Industry

180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

July 2003
OGD

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Contains Nonbinding Recommendations

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I. INTRODUCTION

This guidance is intended to provide information on how the Food and Drug Administration (FDA) intends to determine eligibility for 180-day generic drug exclusivity when, on the same day, more than one applicant submits an abbreviated new drug application (ANDA) for the same drug under section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act) containing a paragraph IV certification to a listed patent, and no paragraph IV certification to the patent was submitted on any previous day. To date, FDA's exclusivity decisions have involved applications or amendments submitted on different days. This guidance explains why and how the Agency intends to apply a *multiple first applicant* approach.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER) in cooperation with the Office of Regulatory Policy (ORP) and the Office of the Chief Counsel (OCC) at the Food and Drug Administration.

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 ANDA approval process, which allows lower-priced generic versions of previously approved innovator drugs to be approved and brought on the market.

An innovator drug applicant must include in its new drug application (NDA) information about any patents that claim the drug product that is the subject of the NDA, or the use of such drug product (21 U.S.C. 355(b)(1) and (c)(2)). The FDA publishes this patent information upon approval of the NDA or a supplemental NDA in *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is generally known as the *Orange Book*.

An ANDA applicant must include in its ANDA a patent certification as described in section 505(j)(2)(A)(vii) of the Act. The certification must make one of the following statements: (1) such patent information has not been filed; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted. The fourth certification is known as a *paragraph IV certification*. The ANDA applicant must provide appropriate notice of a paragraph IV certification 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 (21 U.S.C. 505(j)(2)(B)(i), 21 CFR 314.95). Section 505(j)(5)(B)(iv) of the Act established an incentive for generic manufacturers to file paragraph IV certifications and to challenge listed patents as invalid, or not infringed, by providing for a 180-day period of marketing exclusivity:

> 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, [the font size of this paragraph needs to be 11]
>
> whichever is earlier.

This means that, in certain circumstances, an applicant who submits the ANDA containing the first paragraph IV certification to a patent is *protected from competition* from other generic versions of the same drug product for 180 days after the earliest of either the initial marketing of the first applicant's drug or a court decision that holds that the patent that is the subject of the

paragraph IV certification is invalid or not infringed. This marketing protection is commonly known as *180-day exclusivity*.

III. DISCUSSION

The 180-day period of generic drug exclusivity provides a very strong financial incentive for an ANDA applicant to challenge a patent that it believes it does not infringe or that it believes is invalid or unenforceable. The Congressional Budget Office (CBO) issued a report in July 1998 entitled *How Increased Competition from Generic Drugs has Affected Prices in the Pharmaceutical Industry*. This report indicated that the price of a generic drug decreases with the entry of multiple manufacturers selling generic duplicates of a given innovator drug (see CBO report page 33). With less competition, an ANDA holder is able to derive higher profits. Thus, the opportunity to be the sole competitor to the innovator for up to 6 months is aggressively pursued.

Since the decisions in *Mova Pharmaceuticals, Inc. v. Shalala*, 140 F.3d 1060 (D.C.Cir. 1998) and *Granutec, Inc. v. Shalala*, 46 U.S.P.Q.2d 1398 (4th Cir. 1998), the first applicant who submits a substantially complete ANDA containing a paragraph IV certification to a listed patent is eligible for 180-day generic drug exclusivity.[2] As noted in a 1999 citizen petition response,[3] many of the current regulations were adopted prior to the *Mova* decision, when the Agency interpreted the statute to require that an ANDA applicant had to be sued and win its patent litigation to qualify for exclusivity. FDA's pre-*Mova* interpretation limited the number of times 180-day exclusivity was granted because an ANDA applicant had to be first to challenge a patent and win the patent litigation to be eligible for 180-day exclusivity. The chance of having multiple ANDA applicants qualify for 180-day exclusivity was extremely low as evidenced by the number of times that 180-day exclusivity was granted.[4] By contrast, after the *Mova* decision, it is now easier to qualify for 180-day exclusivity. As a result, FDA has had to address a number of new issues, including eligibility for exclusivity when multiple paragraph IV certifications are filed on the same day.

Congress did not address, in the 180-day exclusivity provisions of the Act, the possibility that multiple applicants would submit patent challenges to FDA on the same day, when no applicant had submitted a challenge to the patent on a previous day. Similarly, FDA regulations now in effect do not address this specific situation. In August 1999, FDA proposed a multiple first applicant approach in a proposed rule addressing 180-day generic drug exclusivity (64 FR 42873; August 6, 1999). FDA received comments both for and against this approach (see Docket 85N-0214). The proposed rule was withdrawn in 2002 for reasons unrelated to the

[2] The regulatory history of this issue has been previously described in the June 1998 CDER guidance for industry *180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*.

[3] See response to 99P-1271/PSA1 and PSA2 issued August 2, 1999.

[4] In the years from 1984 to 1998, only three ANDA applicants qualified for 180-day exclusivity. Since the *Mova* decision in 1999, more than 60 ANDAs have received 180 days of exclusivity.

merits of the multiple first applicant approach (67 FR 66593; November 1, 2002). When the proposed rule was withdrawn, the Agency noted that it would continue to regulate directly from the statute and any applicable regulations, and make decisions on an issue-by-issue basis. The Agency continues to believe that the approach described in the proposed rule is a reasonable and appropriate interpretation of the statute. Two citizen petitions have specifically asked the Agency to follow the approach described in the proposed rule when addressing 180-day exclusivity in cases where there are multiple ANDAs containing challenges to the same patent submitted on the same day (see Dockets 00P-1445 and 03P-0217).

Same day patent challenges generally occur when the expiration of 4 years of a 5-year exclusivity period under section 505(j)(5)(D)(ii) permits submission of ANDAs containing a paragraph IV certification as of a specific date, and multiple applicants vie to be first to make such a submission. Multiple submissions on the same day may also occur when a new patent is issued by the Patent and Trademark Office and submitted to FDA by the NDA sponsor after ANDAs have been submitted. Because new patents must be submitted to FDA within 30 days of issuance, ANDA applicants position themselves to be the first to submit a paragraph IV certification as soon as the patent is submitted to FDA – often exactly 30 days after patent issuance.

Recently, there have been a number of cases in which multiple ANDA applicants or their representatives have sought to be the first to submit a patent challenge by lining up outside, and literally camping out adjacent to, an FDA building for periods ranging from 1 day to more than 3 weeks. Concerns about liability, security, and safety led the property owners to prohibit lines of applicants before the date submissions may be made. This has lent an urgency to the question of how the Agency deals with multiple ANDA applicants submitting paragraph IV certifications on the same day. There are other periods of exclusivity expiring soon, and FDA believes it is possible there will be multiple ANDA submissions referencing the same listed drug. Because of the seriousness of these issues, it has been necessary to promptly provide information to the industry on how patent challenges may be made to FDA and how FDA will apply the 180-day exclusivity provisions of the statute to these submission.

FDA intends to apply a *multiple first applicant* approach to eligibility for 180-day exclusivity by considering all substantially complete ANDAs, amendments, and supplements containing a paragraph IV certification to a listed patent that are submitted to the OGD document room on the same day as being *first applicants,* when no paragraph IV certification to the patent has been submitted on any previous day, as long as the applications comply with the applicable requirements for submission. FDA considers this approach to be an appropriate interpretation of the statutory language and consistent with the goals of the Hatch-Waxman Amendments. This approach will provide all applicants submitting patent challenges on the same day an opportunity to share in exclusivity; it permits submission by U.S. mail or courier or delivery service; it permits, but does not require, submission in person; it avoids the random aspect of a lottery or mail room date stamp approach; it will prevent disputes over *who's first*, which rely on video and other evidence; and it will preserve the safety and security of the applicants and FDA property and staff.[5]

[5] Consistent with FDA's current practice, submission by facsimile or email is ***not*** considered *officially submitted* for purposes of determining the date of submission.

IV. HOW MULTIPLE APPLICANT EXCLUSIVITY WORKS

Under the approach described in this guidance, FDA intends to treat all ANDAs containing a paragraph IV certification to a listed patent that are submitted on the same day as being submitted at the same time for purposes of 180-day exclusivity when no ANDA for the same drug product containing a paragraph IV certification to the same patent has been submitted on a previous day. Thus, none of those same-day submissions would be considered "previous[ly] . . . submitted" to another patent challenge submitted on that same day for purposes of section 505(j)(5)(B)(iv), and all applicants who fulfill the requirements for submission would be considered *first applicants*. The Agency intends to approve a first applicant's ANDA whenever it is ready for approval. Whether and when the Agency will be able to approve a first applicant's ANDA will depend upon a number of factors, including, for example, the status of its scientific submissions to the Agency. Exclusivity begins to run, independent of the approval, with the commercial marketing of that drug product or with a court decision on the patent, whichever comes first. Exclusivity will be triggered for all of the first applicants for a specific listed patent by the earlier of commercial marketing by one of the first applicants or by a court decision (regarding the patent as to which the applicant is a first applicant) finding the patent invalid, unenforceable, or not infringed. The commercial marketing trigger will begin exclusivity as to all of the listed patents; a court decision will only begin the running of exclusivity as to the patents addressed in the decision.

During the exclusivity period, FDA may approve any other first applicant's ANDA, but no other ANDAs. Any first applicant whose ANDA is approved after the exclusivity has been triggered will share in the remaining period of exclusivity. Once the 180-day exclusivity period has run, FDA may approve all subsequent ANDAs.

Obviously, this approach may deprive any one applicant of the chance to be the sole competitor to the NDA holder. But exclusivity is already structured in such a way that eligibility for exclusivity does not guarantee 180 days as the sole marketed generic drug (i.e., the court decision trigger could start exclusivity before an ANDA is approved, or uncertainty over the patent could result in no marketing of an approved product until an affirmation in the Federal Circuit of a district court win). A *multiple first applicant* approach to 180-day exclusivity will limit the number of ANDAs approved during the exclusivity period to the number of first applicants. Moreover, making multiple applicants eligible for exclusivity may give each first applicant some part of the benefit from the early challenge to the listed patent.

The approach to 180-day exclusivity described in this guidance will apply only in cases in which multiple ANDA applicants submit paragraph IV certifications challenging the same listed patent or patents on the same *first* day. The Agency recognizes the highly competitive nature of the generic drug approval process and the possibility of substantial profits for the recipient of 180-day exclusivity. There is no public health reason to encourage and reward competition over being the *first* to submit a paragraph IV certification within minutes or seconds of another such applicant. The Agency believes that, where there are multiple filings on the same first day, the

multiple first applicant approach is consistent with language of section 505(j)(5)(B)(iv) and with the intent of both the 180-day exclusivity provision and the Hatch-Waxman Amendments.

V. IMPLEMENTATION

This guidance is being issued as a level 1 guidance for immediate implementation, consistent with FDA's good guidance practices regulation (21 CFR 10.115). The Agency believes that given the need for public guidance on this pressing issue and existing liability, safety, and security concerns, public comment is neither feasible nor appropriate before implementing this guidance. FDA intends to apply the approach described in this guidance to all 180-day exclusivity determinations made by FDA on or after the date of publication of the notice announcing the availability of this guidance involving situations in which the first paragraph IV certifications to a specific patent are submitted on the same day (including patent certifications that were submitted prior to the date of the notice where the exclusivity determination has not yet been made). The approach described in this guidance will remain in effect until superseded.