

Nature and Scope of the Proposed Regulatory Change

Based on the above, Customs is proposing in this document to revise paragraph (c) of § 113.62 to ensure that it will cover documents and other evidence required in connection with the importation/entry process that are prescribed by, and submitted to, Government agencies other than Customs. Although the need for this proposal arose in the specific context of the FSA end-use certificate program, Customs has drafted the proposed new regulatory language in broad terms because Customs believes that the basic principle at issue should be applicable to importation/entry-related requirements of all Government agencies.

Comments

Before adopting this proposed regulation as a final rule, consideration will be given to any written comments timely submitted to Customs, including comments on the clarity of this proposed rule and how it may be made easier to understand. Comments submitted will be available for public inspection in accordance with the Freedom of Information Act (5 U.S.C. 552), § 1.4, Treasury Department Regulations (31 CFR 1.4), and § 103.11(b), Customs Regulations (19 CFR 103.11(b)), on normal business days between the hours of 9 a.m. and 4:30 p.m. at the Regulations Branch, Office of Regulations and Rulings, U.S. Customs Service, 1300 Pennsylvania Avenue, NW., 3rd Floor, Washington, DC.

Regulatory Flexibility Act and Executive Order 12866

Pursuant to the provisions of the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*), it is certified that the proposed amendment, if adopted, will not have a significant economic impact on a substantial number of small entities. The proposed regulatory amendment will not require any additional action on the part of the public but rather is intended to facilitate Customs enforcement efforts involving existing import requirements under other Government agency laws and regulations. Accordingly, the proposed amendment is not subject to the regulatory analysis or other requirements of 5 U.S.C. 603 and 604. Furthermore, this document does not meet the criteria for a "significant regulatory action" as specified in E.O. 12866.

Drafting Information

The principal author of this document was Francis W. Foote, Office of Regulations and Rulings, U.S. Customs Service. However, personnel from other offices participated in its development.

List of Subjects in 19 CFR Part 113

Bonds, Customs duties and inspection, Imports, Reporting and recordkeeping requirements, Surety bonds.

Proposed Amendments to the Regulations

For the reasons stated above, it is proposed to amend Part 113 of the Customs Regulations (19 CFR part 113) as set forth below.

PART 113—CUSTOMS BONDS

1. The authority citation for Part 113 continues to read in part as follows:

Authority: 19 U.S.C. 66, 1623, 1624.

* * * * *

2. Section 113.62(c) is revised to read as follows:

§ 113.62 Basic importation and entry bond conditions.

* * * * *

(c) *Agreement to produce documents and evidence.* If merchandise is released conditionally to the principal before production of all documents or other evidence required by a law or regulation administered by Customs or another government agency, the principal agrees to furnish Customs or the other government agency with any such document or other evidence as required by, and within the time specified in, such law or regulation.

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Raymond W. Kelly,
Commissioner of Customs.

Approved: June 17, 1999.

John P. Simpson,
Deputy Assistant Secretary of the Treasury.
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 314

[Docket No. 85N-0214]

180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its regulations governing 180-day generic drug exclusivity under the Federal Food, Drug, and Cosmetic Act (the act). The proposed rule clarifies existing eligibility requirements for abbreviated new drug application (ANDA) sponsors and describes new eligibility requirements. The proposed changes to the regulations are necessary because of recent court decisions invalidating portions of FDA's current regulations. The proposed regulations are intended to permit the prompt entry of generic drug products into the market while maintaining the incentive of market exclusivity for generic drug manufacturers.

DATES: Submit written comments by November 4, 1999. Submit written comments on the information collection requirements by September 7, 1999. See section VIII of this document for the effective date of a final rule based on this document.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection requirements to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Virginia G. Beakes, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-2041.

SUPPLEMENTARY INFORMATION:

I. Background

The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (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 a generic version of a previously approved innovator drug to be approved without submission of a full new drug application (NDA). An ANDA refers to a previously approved new drug application (the "listed drug") and relies upon the agency's finding of safety and effectiveness for that drug product.

Innovator drug applicants must include in an NDA information about patents for the drug product that is the subject of the NDA. FDA publishes this patent information as part of the agency's publication "Approved Drug

Products with Therapeutic Equivalence Evaluations" (the Orange Book).

Generic drug applicants must include in an ANDA a patent certification described in section 505(j)(2)(A)(vii) of the act for each patent listed in the Orange Book for the listed drug. The applicant must certify one of the following for each patent: (1) that no patent information on the drug product that is the subject of the ANDA has been submitted to FDA; (2) that such patent has expired; (3) the date on which such patent expires; or (4) that 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. These certifications are known as "paragraph I," "paragraph II," "paragraph III," and "paragraph IV" certifications, respectively.

Notice of a paragraph IV certification must be provided to each owner of the patent (patent owner) that is the subject of the certification and to the holder of the approved NDA (NDA holder) to which the ANDA refers. The terms "patent owner" and "NDA holder" as used throughout this proposed regulation mean either those parties or their representatives, including exclusive licensees. The agency recognizes that different terms are used throughout other sections of the regulations for the idea expressed in section 505(j)(2)(B)(i)(I) and (j)(2)(B)(i)(II) of the act that notice must be given to the principals (patent owner and NDA holder) or their representatives. The agency has added a definitions section to the proposed regulation to clarify the meaning of these terms, as well as other terms, as used in this section.

The submission of an ANDA for a drug product that is claimed in a patent is an infringing act if the ANDA product is intended to be marketed before expiration of the patent. (See 35 U.S.C. 271(e)(2).) Therefore, the submission of an ANDA with a paragraph IV certification may be the basis for patent infringement litigation.

Given this risk of patent infringement litigation, section 505(j)(5)(B)(iv)¹ of the

act provides an incentive for generic drug applicants to file paragraph IV certifications challenging patents that may be invalid, unenforceable, or not infringed by the product that is the subject of the ANDA.

In certain circumstances, the first applicant whose ANDA contains a paragraph IV certification is protected from competition from subsequent generic versions of the same drug product for 180 days from either the date the first applicant's drug product is first commercially marketed or the date of a final court decision holding the patent that is the subject of the paragraph IV certification invalid, unenforceable, or not infringed. This marketing protection is commonly known as "180-day exclusivity."

In the **Federal Register** of October 3, 1994 (59 FR 50338), FDA published the final rule implementing the patent and marketing exclusivity provisions of the Hatch-Waxman Amendments. Section 314.107(c)(1) (21 CFR 314.107(c)(1)), the regulation implementing section 505(j)(5)(B)(iv) of the act, provided:

If an abbreviated new drug application contains a certification that a relevant 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. (Emphasis added)

FDA's requirements for 180-day exclusivity were successfully challenged in the courts in *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), and *Granutec, Inc. v. Shalala*, No. 97-1873 and No. 97-1874, 1998 U.S. App. LEXIS 6685 (4th Cir. Apr. 3, 1998).

Following the *Mova* circuit court decision, on June 1, 1998, the district court entered an order stating that the

successful defense requirement of § 314.107(c)(1) is invalid and permanently enjoined FDA from enforcing it. In the **Federal Register** of July 14, 1998 (63 FR 37890), FDA published a guidance for industry entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act" (June 1998), describing its approach to 180-day exclusivity in light of the court decisions. In the **Federal Register** of November 5, 1998 (63 FR 59710), the agency published an interim rule revoking the "successful defense" requirement. Since that time the agency has regulated directly from the statute when making exclusivity decisions on a case-by-case basis.

The agency is proposing new regulations to address the issues that have arisen as a result of the *Mova* and *Granutec* decisions and to respond to other matters related to 180-day exclusivity not currently addressed by the regulations. Consistent with the legislative purpose of section 505(j)(5)(B)(iv) of the act, the proposed regulations continue to provide an incentive for challenging a listed patent, while at the same time preventing prolonged or indefinite delays in the availability of generic drug products.

During litigation of the many cases related to 180-day exclusivity, the parties and courts have recognized the potential for the 180-day exclusivity process to substantially delay the entry of competitive generic drug products into the market. This situation can occur when the marketing of any subsequent generic drug product is contingent upon the occurrence of an event that is within the first ANDA applicant's control. Such delays could result, for example, from the inability of the first ANDA applicant with a paragraph IV certification to obtain timely approval of its application and begin commercial marketing of its product.

Licensing agreements and other arrangements between an innovator company and the generic drug company who is the first ANDA applicant to file a paragraph IV certification can be of considerable financial benefit to the companies involved, but also may contribute to delayed generic competition by forestalling the beginning, or triggering, of the 180-day exclusivity period. These arrangements can create almost insurmountable barriers to the final approval and marketing of generic drug products that are otherwise ready for final approval. These barriers thwart a major congressional goal underlying the

¹ Section 505(j)(5)(B)(iv) of the act states that:

If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) 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 application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

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.

passage of the Hatch-Waxman Amendments.

In developing the approach described in this proposal, the agency has been guided by the text of the statute, opinions rendered by courts that have addressed these issues, and concerns expressed to the agency in submissions commenting on the June 1998 guidance and November 1998 interim rule. The agency has also been guided by its 15 years of experience with the 180-day exclusivity provisions. This experience has provided FDA with valuable information regarding the influence of the 180-day exclusivity provisions on the ANDA approval process and the marketing of generic drug products.

II. Description of the Proposed Rule

This proposed rule would revise § 314.107 to clarify and modify eligibility requirements for ANDA applicants seeking 180-day marketing exclusivity for a generic drug product. This new approach is offered in light of the courts' rejection of the previous requirement that an ANDA applicant successfully defend against a patent infringement lawsuit before it is eligible for exclusivity.

A. 180-Day Exclusivity Eligibility

1. Only First Applicant is Eligible

The statutory language describing which applications are eligible for 180-day generic drug exclusivity is ambiguous. The current regulation interprets the statute as allowing eligibility for exclusivity only for the applicant that submits the first substantially complete ANDA with a paragraph IV certification. Although the agency has considered alternative interpretations, such as "rolling exclusivity" in which the next-in-line applicant is eligible for exclusivity should the previous applicant become ineligible, FDA proposes to maintain the current interpretation. The agency, however, invites comments related to exclusivity eligibility, both those supporting this interpretation and those suggesting other possibilities.

Under this proposed rule, only the applicant submitting the first substantially complete ANDA for a listed drug with a paragraph IV certification to any patent in the Orange Book for the listed drug (first applicant) would be eligible for exclusivity. A substantially complete application must contain all of the information required under section 505(j)(2)(A) of the act and under 21 CFR 314.50 and 314.94. These requirements include the submission of the results of any required

bioequivalence studies, or, if appropriate, a request for a waiver of such studies. In order for an ANDA to be considered substantially complete for purposes of exclusivity, the bioequivalence studies submitted in the ANDA at the time it is initially submitted must, upon review by the agency, meet the appropriate standards for approval. If the applicant must conduct a new bioequivalence study to obtain approval of the ANDA, the application will not be considered to be substantially complete and the applicant will not be eligible for exclusivity. No other applicant with a paragraph IV certification will be eligible for exclusivity for that drug product. The agency is adopting this position out of concern that, in the rush to be the first ANDA with a paragraph IV, applicants will submit the results of the first completed bioequivalence study, whether or not the results meet the standards for approval. The bioequivalence study is a crucial component of the ANDA and conduct of the studies can be time consuming. In order to prevent the granting of exclusivity on the basis of submission of an inadequate bioequivalence study, FDA has determined that to be eligible for exclusivity, the ANDA applicant must submit, as part of the initial application, a bioequivalence study that meets the standards for approval.

To be eligible for exclusivity, an applicant must be the first to submit ANDA that is both substantially complete and contains a paragraph IV certification to any listed patent. The first applicant can be an applicant that submits an ANDA that initially contains a paragraph III certification, but later amends the certification to a paragraph IV certification, if at the time of the amendment that applicant's ANDA is the first substantially complete ANDA to contain a paragraph IV certification. If the first applicant subsequently withdraws its application or changes or withdraws its paragraph IV certification, either voluntarily or as a result of a settlement or defeat in patent litigation, no ANDA applicant will be eligible for 180-day exclusivity.

Limiting eligibility for exclusivity to the first applicant to submit a substantially complete ANDA with a paragraph IV certification is consistent with the goal of permitting earlier entry into the market of generic competitor products by encouraging prompt challenges to innovator patents. Granting exclusivity to a later applicant that submits a patent challenge, and that only becomes first in line because another applicant(s) has withdrawn its application or paragraph IV certification, would further delay the

entry into the market of generic drug products with no countervailing public benefit.

In addition, if the first applicant submits a new paragraph IV certification because, for example, it makes a formulation change requiring a supplement or an amendment to its ANDA, it may no longer be accorded first applicant status. If there is another applicant with a paragraph IV certification for the same drug product, the first applicant will no longer be eligible for 180-day exclusivity. Also, no other applicant will be eligible for 180-day exclusivity.

As described in the preamble to the 1994 final rule (59 FR 50338 at 50348), there is one exception to this principle. If the agency accepted for filing a substantially complete ANDA prior to the NDA holder's submission of a late (untimely) filed patent, the ANDA applicant is not required to certify to this patent. However, if the ANDA applicant amends its ANDA to include a paragraph IV certification to the untimely filed patent, and the ANDA applicant later withdraws that paragraph IV certification, the next applicant to file a paragraph IV certification to the untimely filed patent will be eligible for exclusivity. The agency believes that in this situation it is appropriate to grant exclusivity to an applicant who was required to file a paragraph IV certification because the applicant filed its ANDA after the NDA holder submitted the patent information.

If there are multiple patents for the listed drug, the applicant submitting the first paragraph IV certification to any of the listed patents will be the only ANDA applicant eligible for exclusivity for that drug. The agency considered an approach that could have made multiple applicants eligible for exclusivity based upon the order of submission of paragraph IV certifications for each patent. Different ANDA's are most likely to have the first paragraph IV certifications to different patents when new patents are listed for the innovator drug after the submission of the first ANDA. Although the statute would support granting multiple exclusivities, the agency has determined that such multiple exclusivities for a single drug could further delay the entry of generic drugs onto the market. For example, if two different applicants were eligible for exclusivity because each was the first to file a paragraph IV certification for a different listed patent, and neither exclusivity could begin to run until first commercial marketing or a favorable court decision, it is possible that each exclusivity would block the final

approval of the other application for a substantial period of time. Moreover, the large number of patents listed for many drugs, the real possibility that different ANDA applicants may submit first paragraph IV certifications for these patents, and the relative ease with which an applicant now becomes eligible for exclusivity could combine to create an exclusivity program that is virtually unworkable in its complexity and which would create even more uncertainty for the industry.

If the ANDA applicant submitting the first substantially complete ANDA with a paragraph IV certification submits paragraph IV certifications to multiple patents at that time, any of those certifications will render the applicant eligible for exclusivity. The first court decision finding one of the patents invalid, not infringed, or unenforceable will trigger the running of the applicant's exclusivity.

2. First Applicant Eligible if Not Sued

The agency is proposing to amend § 314.107(c)(1) to state that the first applicant would be eligible for 180 days of market exclusivity even if the applicant is not sued for patent infringement by the patent owner or NDA holder. This is consistent with the policy established in FDA's June 1998 guidance. It is also consistent with the decision in *Purepac v. Friedman*, 162 F.3d 1201 (D.C. Cir. 1998), in which the court noted that section 505(j)(5)(B)(iv) of the act does not require the first applicant to be sued to be eligible for exclusivity.

The agency recognizes that neither the *Purepac* nor the *Mova* opinion expressly foreclosed the agency from adopting a requirement that an applicant be sued, and that in the 1989 proposed rule FDA considered a "litigation" requirement as a prerequisite for exclusivity eligibility. (See 54 FR 28872 at 28929, July 10, 1989.) However, in light of the removal of the "successful defense" requirement and subsequent reconsideration of the statutory language, the agency proposes that an applicant would be eligible for 180-day exclusivity even if it is not sued by a patent owner or NDA holder.

FDA believes that if the first applicant avoids a lawsuit and the related 30-month stay of final approval (see section 505(j)(5)(B)(iii) of the act), for example, by designing around a patent in such a way that its drug product is clearly noninfringing, then that applicant should not be denied eligibility for exclusivity. In addition, an ANDA applicant should not be encouraged to file a frivolous certification that invites litigation so as to qualify for exclusivity. Permitting an applicant who avoids a

lawsuit to be eligible for exclusivity is consistent with the statutory language and goal of facilitating prompt entry of generic drug products into the market.

3. First Applicant Not Eligible if Sued and Loses Lawsuit

If the first applicant is sued and loses the patent litigation, proposed § 314.107(c)(4) would require the applicant to change its certification from a paragraph IV to a paragraph III. Upon the required certification change, the applicant would lose any claim to exclusivity eligibility.

Nothing in the statute or the regulations supports an award of exclusivity to an ANDA applicant that loses its lawsuit. In fact, such an award would run counter to the statutory goal of promoting earlier entry of generic drug products into the market.

If the agency were to interpret the statute to permit exclusivity for an ANDA applicant that lost its patent litigation, a subsequent applicant that is not sued for patent infringement because it managed to design around the patent nonetheless would not be able to enter the market until after patent expiration. The court decision trigger for the beginning of exclusivity would be unavailable to this subsequent applicant because it applies only when there has been patent litigation as a result of the paragraph IV certification and an ANDA applicant has won.

Additionally, if the agency permitted exclusivity for an applicant that lost its litigation and therefore could not market its product, the innovator might avoid generic competition for the life of its patent merely by refusing to sue any subsequent ANDA applicant. This outcome would not be justified by the first applicant's unsuccessful challenge to the patent.

The declaratory judgment provision discussed in section II.F of this document could prevent an innovator company from using this strategy to completely block ANDA approvals in some cases. However, it is unreasonable to expect subsequent ANDA applicants to obtain a declaratory judgment that triggers exclusivity for a first applicant who has not provided any benefit to the public, merely because the subsequent applicant wants to avoid being blocked for the life of the patent.

If a first applicant that loses its patent suit is not eligible for exclusivity, generic drug products may be able to enter the market prior to expiration of the innovator's patent in several situations. Market entry can occur if a subsequent ANDA applicant with a paragraph IV certification prevails in its patent litigation, settles its patent

litigation, or is not sued as a result of the paragraph IV certification.

The agency recognizes that this approach requires a new interpretation of § 314.94(a)(12)(viii)(A). That provision states that when an applicant changes its paragraph certification from a IV to a III after losing a patent infringement suit, "the application will no longer be considered to be one containing a [paragraph IV] certification." Previously the agency had described that regulatory provision as fulfilling only the "housekeeping" function of informing the agency that the ANDA would not be approved until the patent expired, and explained that the provision had no implications for exclusivity eligibility. That interpretation was consistent with the entire regulatory scheme that was built around the successful defense requirement.

The removal of the successful defense requirement has resulted in a fragmented regulatory framework, forcing the agency to modify not only the regulatory language in certain parts but also, as in this case, its interpretation of language that is to remain. Under the new proposed approach, when a first applicant loses its patent litigation and changes its certification from a paragraph IV to a paragraph III under § 314.94(a)(12)(viii)(A), it would not be eligible for exclusivity. In addition, a voluntary change in patent certification from a IV to a III as described in § 314.94(a)(12)(viii) also would have the effect of rendering the first ANDA applicant ineligible for 180-day exclusivity. After the first applicant changed its patent certification to a III, no applicant would be eligible for exclusivity, and the agency could approve eligible subsequent applications.

4. Shared Exclusivity for Multiple ANDA's Filed on the Same Day

The agency is proposing that all applicants for ANDA's containing paragraph IV certifications for a particular drug product that are received on the same day will be eligible for exclusivity if no other ANDA with a paragraph IV certification for the drug product has been previously filed. All such applicants would be considered first applicants. Submission of ANDA's on the same day is most likely to occur when an innovator's 5-year exclusivity barring FDA acceptance of ANDA's expires, or when ANDA applicants wish to challenge a patent listed for an innovator product with 5 years of exclusivity and file ANDA's at the end of 4 years of exclusivity (see section

505(j)(5)(D)(ii) of the act). The applicable periods would be 5 1/2 years or 4 1/2 years when pediatric exclusivity has been granted (see section 505A(a) of the act (21 U.S.C. 355a(a))).

Under this proposal, the exclusivity period would be shared by all first applicants. Once the exclusivity period begins, it would run for all first applicants, protecting the group of first applicants from competition from later applicants during the 180-day period. The application of the triggering period, discussed in section II.B.1 of this document, would remain essentially the same, with a slight modification. After a triggering event (described in section II.B of this document) occurred, all eligible first applicants could be approved and would be eligible to share the 180-day exclusivity. Once the 180 days of exclusivity has run following the first triggering event, any ANDA that was not among the group of first applicants also would be eligible for final approval.

The agency believes the statutory language supports this approach, which would protect the incentive created by Congress for ANDA applicants to challenge patents. Further, this approach is preferable to alternative approaches. One alternative approach, which the agency does not propose because it does not preserve the incentive to challenge patents, would be for the agency to determine that no ANDA applicant is eligible for 180-day exclusivity if, on the same day, the agency receives more than one ANDA with a paragraph IV certification for the same drug product and no other ANDA with a paragraph IV certification for the drug product has been previously filed.

Another option is for the agency to attempt to determine which application it received first on the same day, an inquiry that is impractical and may result in an arbitrary ordering of applications. It may not be possible for the agency to determine which application was received first. If, for example, the agency received more than one eligible application in the same mail delivery on a particular day, it would be impossible to determine which application was received first. If applications were received by various means throughout the day, when the applications in the pile were retrieved to date-and time-stamp, the application that the agency received first might be stamped last. Although theoretically this particular problem could be avoided by stamping each document at the time of receipt, this solution is impractical given agency workload and resource constraints.

5. Patent Expiration and 180-Day Exclusivity

The agency is clarifying that once the patent for which the first applicant filed a paragraph IV certification expires, the first applicant is no longer eligible for exclusivity. When the first applicant is no longer eligible for exclusivity, FDA may approve all otherwise eligible ANDA's. FDA regulations at § 314.94(a)(12)(viii) currently provide that exclusivity cannot extend beyond the term of the patent.

B. The Results of the Patent Challenge

In general, once an ANDA applicant has submitted a paragraph IV certification and notified the NDA holder and patent owner of the patent challenge under § 314.95 (21 CFR 314.95), a number of outcomes are possible including: (1) The NDA holder or patent owner may sue the ANDA applicant within the 45-day period established by statute (section 505(j)(5)(B)(iii) of the act) and that suit may be litigated to final judgment, (2) the parties may reach a settlement either before or after a patent infringement lawsuit is filed, or (3) the NDA holder and patent owner may refrain from filing a patent infringement suit. Which of these events occurs will depend on many factors, including market considerations and the relative strength of the patent claims. However, in each of these cases, there is the potential for a substantial delay in the entry of generic drug products into the market. The agency is proposing a relatively simple approach to limiting this delay, one that applies generally to all of the outcomes described previously.

Under the current 180-day exclusivity approach, delays in the approval of competitive generic drug products are the result of delays in the occurrence of one of the two events (triggering events) that will trigger the beginning of the 180-day exclusivity period—either the first commercial marketing of the first applicant's product, or a decision of a court holding the patent invalid, not infringed, or unenforceable, whichever is earlier. The courts in the *Mova* and *Purepac* decisions suggested that, to prevent unreasonable delay in the final approval of subsequent generic drug applications, FDA could require that a first ANDA applicant bring its product to market—and thus begin the running of exclusivity—within a prescribed time period. The agency believes that such a requirement is appropriate.

1. Triggering Period

The agency proposes to adopt the approach suggested by the courts in the

Mova and *Purepac* decisions and set a time limit for the exercise of exclusivity. The agency is proposing the use of a 180-day "triggering period," during which there must either be a favorable court decision regarding the patent or the first applicant must begin commercial marketing of its product. If neither of these events occur during the triggering period, the first applicant will lose its eligibility for exclusivity and subsequent ANDA's will be eligible for immediate approval.

The term "triggering period" is used throughout this proposed rule to refer to the 180-day period described previously; this is distinct from the 180-day exclusivity period (see section II.B.4 of this document) that may follow the triggering period. The term "trigger" as used throughout this proposed rule refers to the two statutory conditions, one of which must be met, for exclusivity to begin (see section 505(j)(5)(B)(iv) of the act). Those conditions, as discussed in sections I and II.B of this document, are: (1) A court decision finding the patent to be invalid, unenforceable, or not infringed by the ANDA product, and (2) first commercial marketing of the ANDA product. The term "triggering event" in this proposed rule refers to the occurrence of one of the two statutory triggers.

In most cases, the triggering period would begin to run on the day a subsequent ANDA applicant with a paragraph IV certification receives a tentative approval stating that but for the first applicant's exclusivity, the subsequent ANDA would receive final approval. In three instances the triggering period would not begin to run on the date of the tentative approval.

First, if the first applicant was sued for patent infringement as a result of its paragraph IV certification and the litigation is ongoing, the triggering period would not begin until expiration of the 30-month stay of ANDA approval (see section II.B.3 of this document). Similarly, if a court issued a preliminary injunction prohibiting the first applicant from commercially marketing its drug product, the triggering period would not begin until the injunction expired. Finally, the triggering period would not begin until expiration of the statutorily described time period corresponding with any existing exclusivity periods for the listed drug (see sections 505(j)(5)(D)(ii) and 505A(a) of the act).

To determine how a triggering period would work, the agency reviewed its experience with the 180-day exclusivity provision. In the past, delays in obtaining a court decision, or delays in the first applicant gaining approval for

its ANDA and/or bringing its product to market, have generally become a matter of concern when at least one subsequent ANDA applicant has obtained a tentative approval and the only barrier to final approval is the first applicant's eligibility for 180 days of exclusivity. Every day after the tentative approval during which the subsequent applicant can not market its product represents a lost opportunity both for the subsequent applicant and the consumer. The subsequent applicant can not benefit from having submitted an ANDA that meets the requirements of section 505(j) of the act, and the consumer does not have access to one or more lower cost generic products.

Where the first ANDA applicant is eligible for exclusivity and only that eligibility is blocking final approval of a subsequent ANDA, it is appropriate to begin the triggering period on the day that a subsequent applicant has received tentative approval for its ANDA. This is the first day that the absence of a generic drug product from the market is directly linked to the first applicant's eligibility for exclusivity.

a. *Length of triggering period.* The agency is proposing that the triggering period be 180 days. As described previously, the 180-day period would follow one of the following: (1) The tentative approval of a subsequent ANDA with a paragraph IV certification for the same drug product, (2) expiration of a 30-month stay of ANDA approval due to patent litigation, (3) expiration of a preliminary injunction prohibiting marketing of an ANDA product, or (4) expiration of the statutorily described exclusivity periods for the listed drug.

Once the triggering period begins, the ANDA applicant eligible for exclusivity would have 180 days to trigger its exclusivity. This may be done by beginning commercial marketing of its drug product or obtaining a favorable court decision (in its own or other litigation regarding the same patent). Once triggered, the ANDA applicant's exclusivity would then run for 180 days. If, within the 180-day triggering period, the beginning of exclusivity was not triggered, the first applicant would no longer be eligible for exclusivity and the agency could approve subsequent ANDA's at the end of the triggering period.

It is possible that there could be no generic drug product marketed during the triggering period if the first applicant does not begin commercial marketing of its product. In this case, at least one generic drug product—the product that had received the tentative approval—would receive final approval

upon expiration of the triggering period and could begin marketing.

b. *Basis for length of triggering period.* The 180-day length of the triggering period is derived from the statutory provision governing 180 days of exclusivity. This provision quite clearly allows (and Congress, therefore, presumably contemplated) the possibility of a 180-day period during which there is no generic drug product on the market. This would occur when the running of the 180-day period of exclusivity has begun with a court decision finding the patent invalid, unenforceable, or not infringed, but the applicant that has the exclusivity does not begin marketing its product because it is not approved or for another reason.

There is no statutory requirement that the running of the exclusivity triggered by the court decision described in section 505(j)(5)(B)(iv)(II) of the act be accompanied by the commercial availability of the generic drug product. Even if no generic drug product is being marketed, the statute prohibits the agency from approving another ANDA until the 180-day exclusivity period has elapsed. After that period, however, the statute permits the approval of any otherwise eligible ANDA, even if the first applicant never marketed its product. It is therefore reasonable to assume that Congress thought that a 180-day period during which no generic drug product is marketed was acceptable.

At the same time, there is no indication that Congress would countenance an indefinite delay in the marketing of low cost generic drug products once the legal barriers to their approval have been removed. To the contrary, such a scenario directly conflicts with the goals of the Hatch-Waxman Amendments. Therefore, the agency is proposing a 180-day triggering period during which a triggering event must occur to commence the eligible ANDA applicant's period of exclusivity.

The agency recognizes that in very rare cases there could be a time period longer than 180 days during which no generic drug product is available. This may happen if, for example, a court decision triggering the exclusivity period is issued at the end of the 180-day triggering period, and the first applicant does not market its product or waive its right to exclusivity during the resulting 180-day exclusivity period. In the extreme case, this scenario could result in the inability of a subsequent ANDA applicant to market its product for a 360-day period (180-day triggering period plus 180-day exclusivity period) after its tentative approval.

The agency believes, however, that a first applicant that is unable to market its own product at the time a subsequent ANDA applicant receives a tentative approval would ordinarily waive its exclusivity (see section II.H of this document). This would permit final approval of the subsequent ANDA. Moreover, in contrast to the current regulatory structure, under which generic drugs may face almost insurmountable barriers to market entry, the proposed approach provides for much earlier market entry. Under the triggering period approach, there is certainty that one or more generic drug products will be able to enter the market after the 12-month period described previously, and in most cases, much more promptly.

2. Alternative Length of Triggering Period in Specific Cases

The agency is also specifically seeking comment on an alternative approach. The agency is considering shortening the length of the triggering period to 60 days in some cases. The 60-day triggering period would apply to an ANDA applicant that already has received final approval at the time of the tentative approval of a subsequent ANDA, and either has not been sued as a result of its patent certification, or has been sued and the case was settled or dismissed without a decision on the merits of the patent claim. The possible 60-day triggering period in this case is based upon limited data from a July 1998 Congressional Budget Office study entitled "How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry," and a March 1999 internal FDA study (available in Docket No. 85N-0214).

FDA does not consider this 60-day timeframe to be burdensome to ANDA applicants because the data suggest that, since passage of the Hatch-Waxman Amendments, first generic drug products generally reach the market promptly after approval. Specifically, the studies indicate that generic products are routinely marketed within a 2-month period following ANDA approval.

3. Relationship of Triggering Period to 30-Month Stay

When the first applicant to submit an ANDA with a paragraph IV certification is sued by the NDA holder or patent owner, it would be unreasonable to start the triggering period with the tentative approval of a subsequent applicant if the tentative approval was granted relatively soon after the first applicant's patent litigation began. The first

applicant could find it difficult or impossible to either obtain a final court decision in a patent infringement case or begin commercial marketing of its product within 180 days of the subsequent applicant's tentative approval. The first applicant who is sued for patent infringement is, however, provided with a statutory time period, as discussed in the following paragraphs of this document, during which to resolve the patent litigation before the triggering period will begin.

The generic drug product approval process described in the Hatch-Waxman Amendments establishes a 30-month period for resolution of patent litigation resulting from a patent certification. (See section 505(j)(B)(5)(iii) of the act.) During this period, FDA may not approve the ANDA that is the subject of the litigation. After the 30-month period, barring a court order, FDA may grant final approval to the ANDA that is the subject of the litigation. Therefore, the agency is proposing that when the first ANDA applicant is sued as a result of its paragraph IV certification and the patent litigation is ongoing, the triggering period would not begin at least until the 30-month period has lapsed. After the 30 months has passed, the triggering period would begin when a subsequent applicant received a tentative approval. If a subsequent applicant received a tentative approval during the 30-month stay, the 180-day triggering period would begin on the day the 30-month period expired. The first applicant then would have to begin marketing its product, or obtain a final court decision, during the 180-day triggering period to obtain its exclusivity.

4. Distinction Between Triggering Period and Exclusivity Period

Although the triggering period would not begin until expiration of the first applicant's 30-month stay, it is still possible for the exclusivity period to begin during that 30-month period. If, for example, a court issues a favorable final decision in litigation over a subsequent ANDA's patent challenge during the 30-month stay of the first applicant, the exclusivity period for the first applicant would start on the date of that decision.

In proposing this interpretation of the statute—that the triggering period does not begin until expiration of the 30-month stay—the agency is aware that in some cases patent litigation resulting from a paragraph IV certification does not result in a final court decision within 30 months. The agency is also aware that parties to patent litigation in some cases may not have strong

incentives to resolve the litigation as promptly as possible. This proposed approach may alter those incentives and encourage swifter resolution of litigation.

Although the agency is proposing that the general rule will be that the first ANDA applicant has 30 months in which to resolve its patent litigation before the triggering period may start, the agency also would allow for a reasonable extension of this period under certain circumstances. This would occur when the court hearing the patent infringement case issues a preliminary injunction prohibiting the marketing of the drug product that is the subject of the challenged ANDA until there is a court decision finding the patent invalid, not infringed, or unenforceable. The issuance of such an order is contemplated in section 505(j)(5)(B)(iii)(III) of the act.

FDA expects that an injunction would issue upon a finding that it is warranted by the facts and law in the particular case, and that the parties have reasonably cooperated in expediting the action. In the event the court issues an injunction prohibiting the marketing of the drug product under the first ANDA, the triggering period would not begin at least until the injunction expires or is lifted by the court. If the 30-month stay is shortened or lengthened by the court because either party has failed to reasonably cooperate, the triggering period will begin with reference to the date ordered by the court.

While the triggering and exclusivity periods are related, they are also distinct. The exclusivity period starts with either first commercial marketing of the first applicant's generic drug product or with a court decision finding the patent invalid, unenforceable, or not infringed. The triggering period, in contrast, would be tied to the date of a subsequent ANDA's tentative approval, and in some cases to the completion of a 30-month stay. The triggering period may not result in an exclusivity period for the first applicant if no triggering event occurs during the triggering period. In contrast, an exclusivity period may begin independent of any triggering period, if no subsequent ANDA is given a tentative approval to begin the triggering period. Alternatively, the exclusivity period could begin during the triggering period.

C. A Decision of a Court

FDA's current regulations state that for purposes of applying the ANDA approval and exclusivity provisions of the statute, "the court" is the court that enters final judgment from which no appeal can be or has been taken (district

or appellate court) (§ 314.107(e)). This interpretation was challenged in *TorPharm v. Shalala*, No. 97-1925, U.S. Dist. LEXIS 21983 (D.D.C. Sep. 15, 1997); appeal withdrawn and remanded, 1998 U.S. App. LEXIS 4681 (D.C. Cir. Feb. 5, 1998); vacated No. 97-1925 (D.D.C. April 9, 1998).

Plaintiffs in that case maintained that "the court" meant the district court and that final approval could be granted and exclusivity begin running upon the entry of a district court decision finding a patent invalid, unenforceable, or not infringed. Because the district court decision in *TorPharm* agreeing with plaintiffs was vacated (set aside or rendered void), the agency will not address it further in this proposed rule. FDA instead proposes to maintain its current interpretation. The agency believes this interpretation is most consistent with the statutory scheme.

The agency is also proposing that the decision of a court that may begin the running of exclusivity is the final decision of a court hearing any litigation involving the patent at issue. Current § 314.107(c)(1)(ii) states that one of the two exclusivity triggers is the "date of the decision of the court holding the relevant patent invalid, unenforceable, or not infringed." FDA proposes to modify § 314.107(c)(1)(ii) to read the "date of the decision of a court * * *."

This modification is consistent with the statutory language in section 505(j)(5)(B)(iv) of the act. The agency is clarifying that for purposes of both the modified regulatory provision and section 505(j)(5)(B)(iv)(II) of the act, "a decision of a court in an action described in [section 505(j)(5)(B)(iii) of the act] holding the patent which is the subject of the certification to be invalid or not infringed" can be a decision of any court hearing a patent infringement or declaratory judgment case involving the patent at issue. The decision triggering exclusivity need not come from the court hearing the patent litigation involving the first ANDA. (See also *Granutec, Inc. v. Shalala*, 1998 U.S. App. LEXIS 6685, Nos. 97-1873, 97-1874, slip op. at 14-18 (4th Cir. Apr. 3, 1998) (unpublished opinion discussing the agency's interpretation of "a" court decision).)

The use of different language in subsections (I) and (II) of section 505(j)(5)(B)(iv) of the act supports this interpretation. In subsection (I), the statutory trigger is specifically tied to the date that "the applicant under the previous application" gives notice that its product is being commercially marketed. In contrast, the trigger in subsection (II) relates only to the date of "a decision of a court" in patent

litigation described in section 505(j)(5)(B)(iii) of the act.

The language of the first trigger refers to a particular applicant. In contrast, the language of the second trigger does not attach importance to the specific applicant. It instead refers generally to a type of court decision. In the absence of specific, controlling language to the contrary, the agency continues to interpret "a decision of a court" in subsection (II) to mean a decision of any court hearing a patent infringement or declaratory judgment case involving the patent at issue.

This interpretation of the court decision trigger encourages prompt litigation of patent issues by all ANDA applicants, and under some circumstances could result in a corresponding earlier start of the 180-day exclusivity period. This could result in situations where, although the first applicant was sued first, its litigation is not completed first, and its exclusivity begins to run while it is still in litigation.

The agency is aware that in some instances the first applicant may be unable or unwilling to market its product upon satisfaction of the court decision trigger involving another applicant. For example, the first applicant's own patent litigation may be ongoing and its ANDA may have been finally approved at the completion of a 30-month stay under section 505(j)(5)(B)(iii) of the act. However, the applicant may be unwilling to assume the risk of liability for damages by marketing before patent expiration or a court decision finding the applicant's product does not infringe the patent. The agency notes, however, that in such a situation the first applicant may obtain a financial benefit from the award of exclusivity by waiving its exclusivity with respect to a subsequent applicant (see section II.H of this document).

A contrary interpretation that required the court decision be a decision in patent litigation against the first applicant could, under some circumstances, delay entry into the market of drug products by all ANDA applicants. For example, the patent owner or NDA holder may elect not to sue the first ANDA applicant, in which case the court decision trigger would never apply to that applicant's patent challenge, and exclusivity could therefore begin running only with the first applicant's commencement of commercial marketing. If the first applicant's marketing is delayed because it cannot obtain final approval of its ANDA or, having obtained final approval, the first applicant either cannot or will not bring its product to

market, there could be a substantial delay in marketing of any generic drug product. This delay would result even if a subsequent applicant is successful in challenging the patent, either in a lawsuit brought by the innovator or in a declaratory judgment action.

As described in section II.B.3 of this document, under the approach proposed in this rule, the triggering period would not apply when a subsequent applicant obtains a court decision that begins the period of exclusivity. In such cases the first applicant's exclusivity would begin to run on the date of the final court decision in the subsequent applicant's litigation. The triggering period applies only when a subsequent applicant has obtained a tentative approval where final approval is blocked by the first ANDA applicant's eligibility for exclusivity. Under these circumstances, the subsequent applicant would have been eligible for final approval because either: (1) it wasn't sued by the innovator, (2) it was sued but the litigation was settled or dismissed without a favorable court decision, or (3) it was sued and the 30-month stay had elapsed.

D. Settlement Agreements

Settlement agreements are not addressed in current regulations but were discussed in the preamble to the proposed rule of July 10, 1989 (54 FR 28872). In the preamble, FDA explained that the "date of a decision of a court holding the patent invalid or not infringed" in § 314.107(c)(1)(ii) is the "date of a final decision of a court from which no appeal can or has been taken, or the *date of a settlement order or consent decree signed by a Federal judge, which enters final judgment and includes a finding that the patent is invalid or not infringed*" (54 FR 28872 at 28895 (emphasis added)).

FDA is proposing regulations in part to address the most challenging issue with respect to 180-day exclusivity: settlement and licensing agreements between innovator and generic drug companies. These agreements potentially can be made at any stage in the ANDA process, including before an ANDA is filed, after ANDA filing but during the 45-day period within which a patent infringement suit must be brought, after the 45-day period expires but before the first applicant commences commercial marketing, or during patent litigation.

The proposed regulations, by applying the triggering period, would reduce the delay in market entry of generic drug products that can result from such agreements. Although

agreements may still be made, their effect on generic competition would be limited by the requirement that, within 180 days of the first tentative approval of a subsequent ANDA, the first ANDA applicant begin commercially marketing its own product or obtain a favorable court decision.

The agency has seriously considered the suggestions made in comments on the November 1998 interim rule (Docket No. 85N-0214) and the June 1998 guidance (Docket No. 98D-0481). Comments suggested that the agency require that it be promptly notified of a settlement or other agreement that either alters the adversarial relationship between the first ANDA applicant and the patent owner or NDA holder, or from which the first ANDA applicant derives an economic benefit. A number of comments suggested that the agency consider such arrangements as either rendering the first applicant ineligible for exclusivity, or triggering the running of the exclusivity period on the theory that such agreements are akin to commercial marketing.

The agency, however, believes the "triggering period" approach is preferable. This approach would not require FDA to inquire into the business arrangements between pharmaceutical companies, it would not require the submission of any additional information by the ANDA applicant, and it is a clear and definite approach that relies upon publicly available information, i.e., the issuing of a tentative approval letter.

E. Prompt Approval and Marketing

Current § 314.107(c)(3) requires a first applicant to actively pursue approval of its ANDA, or the agency may immediately approve any subsequent ANDA eligible for final approval. The agency proposes to delete this requirement because it is unnecessary under the regulatory scheme described in this proposed rule. The new scheme would provide a specific, clearly defined 180-day triggering period, during which the first ANDA applicant must either: (1) Commercially market its drug product, or (2) obtain a favorable court decision regarding the patent.

Given this approach, the issue of whether an ANDA applicant actively pursues approval of its product would not be relevant. The proposed approach, therefore, also has the advantage of eliminating the requirement for the agency to scrutinize applicants' progress and responses during the ANDA approval process, as well as to maintain a standard for active pursuit of approval.

F. Declaratory Judgment

Current regulations implementing the Hatch-Waxman Amendments do not address the application of section 505(j)(5)(B)(iv) of the act to declaratory judgment actions as referred to in section 505(j)(5)(B)(iii) of the act. These proposed regulations address the issue of whether a ruling in a declaratory judgment action brought by the ANDA applicant is a "decision of a court in [an] action described in [section 505(j)(5)(B)(iii)] holding the patent which is the subject of the certification to be invalid or not infringed" (section 505(j)(5)(B)(iv) of the act).

FDA proposes in § 314.107(f)(2)(ii) that a "decision of a court" should include a nonappealable decision of a court in a declaratory judgment action finding the patent invalid, unenforceable, or not infringed.

The agency has considered the suggestion that a dismissal of a declaratory judgment action under certain circumstances be treated as a decision of a court and trigger the 180-day exclusivity period under section 505(j)(5)(B)(iv)(II) of the act. Specifically, the agency considered whether dismissal for lack of jurisdiction on the grounds that no "case or controversy" exists because, for example, a party has no reasonable apprehension of a patent infringement action, could be considered a triggering court decision. The agency has rejected this interpretation of the statute. It places a burden on the agency to inquire into the facts underlying the dismissal of a case, and would be unnecessary under the "triggering period" approach. With the application of the 180-day triggering period, a subsequent applicant who is not sued for patent infringement and obtains a tentative approval with just the first applicant's eligibility for exclusivity serving as a bar to final approval will not be blocked indefinitely from approval.

G. Effect of Dismissal of Litigation

Proposed § 314.107(g) states that the 30-month stay of ANDA approval would not apply once paragraph IV related patent litigation involving the ANDA applicant and patent owner or NDA holder is dismissed without a court decision on the merits of the patent claim, regardless of whether such dismissal is with or without prejudice (whether the claims may be relitigated). The 30-month period, described in section 505(j)(5)(B)(iii) of the act and § 314.107(b)(3)(A) of the regulations, is intended to give innovator companies assurance that generic manufacturers would not file ANDA's with paragraph

IV certifications and then immediately market the approved generic drug product. (See 130 Congressional Record H9118 (daily ed. Sept. 6, 1984) (statement of Rep. Waxman).)

The legislative history of the amendments makes clear that the 30-month stay of approval was intended to correspond as closely as possible with the expected duration of a patent infringement suit, and to provide protection to innovator companies during that time. (See 130 Congressional Record S10504 (daily ed. Aug. 10, 1984) (statement of Sen. Hatch).) Those concerns are not implicated when the litigation is dismissed either as a result of a settlement or licensing agreement, or because the patent owner or NDA holder has determined not to pursue the litigation. Once the litigation is settled, the application can be approved immediately.

H. Waiver of 180-Day Exclusivity and Relinquishing Eligibility

Although current regulations do not address an ANDA applicant's ability to waive its 180-day exclusivity to permit approval of the ANDA of a subsequent applicant(s), the general issue of exclusivity waivers was addressed in the preamble to the 1994 final rule with respect to analogous provisions. There the agency stated that new drug exclusivity under the Hatch-Waxman Amendments can be waived by the holder of the exclusivity (59 FR 50338 at 50359).

Since publication of the 1994 regulations addressing 180-day exclusivity, FDA has been asked to determine whether an applicant who has obtained 180 days of exclusivity can waive such exclusivity to permit approval during the exclusivity period of a subsequent ANDA, or ANDA's, containing a paragraph IV certification. The agency has determined that waiver of 180-day exclusivity, like waiver of new drug exclusivity, is permitted under the act and at least one ANDA applicant has successfully effected a waiver. That waiver was challenged unsuccessfully in *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1 (D.D.C. 1997).

Proposed § 314.107(e) would permit the ANDA applicant that has obtained 180 days of exclusivity with the occurrence of a triggering event under section 505(j)(5)(B)(iv)(I) or (j)(5)(B)(iv)(II) of the act to notify FDA during the period of exclusivity that it will waive its exclusivity in favor of a subsequent ANDA or ANDA's containing a paragraph IV certification. After receiving such notification, the agency may approve the eligible named

ANDA or ANDA's as of the date(s) identified in the notice. Waiver of exclusivity permits ANDA applicants that have been awarded exclusivity, but are either unwilling or unable to market their products, to nonetheless obtain a benefit from that exclusivity. A waiver may be particularly appropriate, for instance, when the first ANDA applicant is sued and, while its litigation is ongoing, a favorable court decision is rendered in a case involving a subsequent applicant. Exclusivity would be awarded to the first applicant, with the 180-day period starting on the date of a final court decision in the subsequent applicant's litigation. The first applicant's ANDA may not be finally approved, however, and the applicant could not market its product. Under these circumstances, the first applicant may obtain a benefit by waiving its exclusivity period in favor of a subsequent applicant.

It should be noted that an applicant may selectively waive its exclusivity only after the 180-day exclusivity period has begun to run with the occurrence of one of the triggering events described in section 505(j)(5)(B)(iv) of the act and in the regulations. Before that time, the first applicant is only eligible for exclusivity and might not obtain exclusivity if, for example, it failed to trigger the exclusivity before the expiration of the triggering period.

Prior to the occurrence of a triggering event, the first applicant may relinquish its eligibility for exclusivity entirely, and by so doing would permit the agency to approve immediately any subsequent ANDA's that are eligible for approval. It may not, however, waive its exclusivity in favor of a specific applicant(s).

I. Multiple Strength/Drug Product Exclusivity

The question of whether the agency will grant a separate period of exclusivity for each strength of a drug product is not addressed in the preambles to the 1989 proposed or 1994 final rules, or in current regulations. A citizen petition (Docket No. 99P-0792) that pertains to this issue was filed on March 31, 1999. The agency has determined that each strength of a drug product can be independently eligible for exclusivity. Applicants may be eligible for a separate exclusivity period for each particular strength of the drug product in an ANDA when each strength refers to a different listed drug.

FDA believes that this form of exclusivity is consistent with the statutory framework and public policy. Under the Hatch-Waxman Amendments, the agency requires that

an ANDA reference a particular listed drug product. Among other requirements, an ANDA applicant must include in the ANDA "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 * * *" (section 505(j)(2)(A)(iii) of the act, emphasis added). The agency, therefore, has determined that each strength of a drug product is itself a listed drug.

FDA's current regulations treat each strength of a drug product as a separate listed drug. Section 314.92(a)(1) (21 CFR 314.92 (a)(1)) states that ANDA's are suitable for "drug products that are the same as a listed drug." The regulation further explains that "the term 'same as' means identical in active ingredient(s), dosage form, strength, route of administration, and conditions of use * * *."

FDA recognizes that different strengths of the same drug product in the same dosage form may be formulated differently for a variety of reasons. Varying formulations of the different strengths may provide separate and distinct bases for patent challenges. Consequently, the result of patent infringement litigation related to one strength of a particular drug product may not be applicable to another strength of the same drug product, even for the same ANDA applicant.

When the agency grants exclusivity to an ANDA applicant under the provisions of section 505(j)(5)(B)(iv) of the act, it may not grant final approval to other ANDA applicants for a period of 180 days. Exclusivity, therefore, affects the remaining applicants by essentially imposing a block on their immediate entry into the market.

The agency's interpretation of the statute to render ANDA's eligible for exclusivity for each particular strength of a drug product would have two results. First, it would encourage applicants vying for submission of the first application, and the concomitant reward of exclusivity, to submit ANDA's that cover the greatest number of strengths in an attempt to obtain maximum protection from other generic competitors. Second, it would prevent an ANDA applicant for only one strength of a drug product from blocking subsequent applicants with other strengths of the drug product from entering the market. Thus, FDA's interpretation would encourage prompt entry into the market of the greatest number of strengths of a particular drug product.

FDA has also determined that when the submission of a new strength of a drug is approved as a result of a

suitability petition, the first ANDA referring to the approved petition that contains a paragraph IV certification to any patent for the listed drug referred to in the petition under § 314.93(d) will be eligible for exclusivity. The new strength of the drug product may have an independent basis for challenging the applicability of a listed patent and therefore should be eligible for the incentive provided by exclusivity.

III. Proposed Implementation Plan

The agency proposes that any final rule based on this proposal take effect 30 days after its publication in the **Federal Register**. The agency proposes to apply the provisions of any final rule to ANDA's pending as of the effective date and to ANDA's that are submitted after that date.

IV. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Title II of the Unfunded Mandates Reform Act requires that agencies prepare a written assessment and economic analysis of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million (adjusted annually for inflation) in any one year.

The agency believes that this proposed rule is consistent with the regulatory philosophy and principles set out in the Executive Order. Because the proposed rule does not impose any mandates on State, local, or tribal governments or the private sector, that

will result in an expenditure in any one year of \$100 million or more, FDA is not required to perform a cost/benefit analysis according to the Unfunded Mandates Reform Act. With respect to the Regulatory Flexibility Act, because this proposed rule may have a significant economic effect on a substantial number of small entities, the analysis set forth below constitutes the agency's Initial Regulatory Flexibility Analysis. Discussion of the expected aggregate costs of this proposed rule and the anticipated impact of the rule on small entities is provided in the analysis. FDA has not identified any other Federal rules that duplicate, overlap, or conflict with the proposed rule.

A. Background

The Hatch-Waxman Amendments benefit consumers by bringing lower priced generic versions of previously approved drugs to market, while simultaneously promoting new drug innovation through the restoration of patent life lost during regulatory proceedings. The award of a 180-day period of market exclusivity for certain ANDA applicants with paragraph IV certifications was designed to maintain this balance by rewarding generic firms for their willingness to challenge unenforceable and invalid innovator patents, or design noninfringing drug products. Recently, however, this balance has been upset and generic competition impeded, in part through the establishment of certain licensing agreements or other commercial arrangements between generic and innovator companies.

Under current regulatory provisions, the first generic applicant to file a substantially complete ANDA with a paragraph IV certification can delay generic competition by entering into certain commercial arrangements with an innovator company. The result may be that, notwithstanding the intent of the Hatch-Waxman Amendments, rewards are directed to generic companies for hindering rather than speeding generic competition. A necessary condition for such arrangements is that the economic gains to the innovator from delaying generic competition exceed the potential economic gains to the generic applicant from 180 days of market exclusivity. Such instances are becoming more frequent because a successful strategy to extend market exclusivity can mean tens of millions of dollars in increased revenue for an innovator firm. Under such circumstances, it can be mutually beneficial for the innovator and the generic company that is awarded 180

days of generic exclusivity to enter into agreements that block generic competition for extended periods. This delayed competition harms consumers by slowing the introduction of lower priced products into the market and thwarts the intent of the Hatch-Waxman Amendments.

FDA's proposal to establish a 180-day triggering period addresses this problem in several ways. In most cases, the first generic applicant with a paragraph IV certification would lose its claim to 180-day exclusivity if it withheld its drug product from the market, or failed to obtain a favorable court decision, for more than 180 days after the tentative approval of a subsequent generic applicant for the same drug product. Also, a subsequent generic applicant could not be blocked from marketing its drug product for longer than, at most, 1 year from when it received tentative approval (the 180-day triggering period plus the 180-day exclusivity period). As a result, the potential economic losses to consumers from the increased unavailability of lower priced generic products would be reduced significantly.

Moreover, decreasing the length of time that these commercial arrangements could block generic competition lessens the market incentive for entering into such agreements. Limiting the period during which an agreement between an innovator and the first generic ANDA applicant with a paragraph IV certification could block generic competition provides less incentive, and therefore makes it less likely, that an innovator and a generic company would enter into such an agreement. Consequently, consumers would benefit because commercial arrangements to block generic competition would be not only less damaging, but would be less likely to occur.

B. Affected Entities

FDA does not know the precise number of businesses, either large or small, that engage in the types of business arrangements that would be significantly affected by the proposed rule. According to standards established by the Small Business Administration, a small pharmaceutical manufacturer employs fewer than 750 employees. While the innovator firms that are affected by the rule are likely to be large businesses, some of the affected generic firms may be small businesses. In 1997, 431 generic product approvals (including different product strengths) were distributed among 96 pharmaceutical companies. The 64 applications that became first generic

approvals for a specific brand name drug, however, were submitted by only 30 firms. Moreover, the 14 first generic approvals that included a paragraph IV certification were submitted by only 5 firms. Therefore, FDA estimates that up to five generic firms and a similar number of innovator firms per year could be financially harmed by the accelerated competition brought about by this rule. Based on a sample of 150 generic firms, the agency could identify fewer than 10 percent that employed over 750 employees. Thus, FDA tentatively projects that approximately five small firms per year, those with first generic approvals containing paragraph IV certifications, could be adversely affected by the increased generic competition. Because this estimate is uncertain, however, FDA invites comments from firms that believe they would be affected by the proposed rule.

C. Compliance Requirements and Costs

To comply with this rule, affected firms will need to learn the new regulatory approach described in this proposed rule. The cost of this proposed rule is difficult to estimate because the number of firms affected is uncertain.

The agency expects, however, that many more firms would benefit from this new approach than would be adversely affected. Because the primary result of the rule would be to speed the start of the 180-day exclusivity period, only those relatively few innovator and generic firms that would profit from delayed competition would be disadvantaged. In contrast, a substantial number of generic competitors would benefit from the earlier sales revenues generated by the quicker introduction of generic competition.

Any professional skills necessary for implementation of this proposal should already exist within the firms and should not need to be newly acquired.

D. Minimizing the Impact on Small Entities

FDA has considered alternatives to regulating 180-day generic drug marketing exclusivity that may have a lesser or different impact on small businesses. Specifically, the agency considered continuing to regulate directly from the statute as it has done since June 1, 1998, when the D.C. District Court enjoined FDA from enforcing its "successful defense" regulation. The agency also considered proposing several modifications to the existing regulations to limit the ability of innovator and generic drug companies to enter into agreements that could thwart congressional intent to

facilitate prompt entry of generic drugs into the market.

The agency considered retaining its current regulations and addressing new regulatory issues by reference directly to the statute. Because of the significant disadvantages associated with this alternative, the agency has rejected it. This alternative would create uncertainty in the generic drug manufacturing industry because the agency anticipates it may take years to provide sufficient guidance while addressing each scenario on an individual basis.

Regulating from the statute on a case-by-case basis also could result in significant delays in entry of generic drug products into the market, because it could limit the means for FDA to prevent such delays. For example, in cases where the first ANDA applicant with a paragraph IV certification was sued by the patent owner or NDA holder, the ANDA applicant and the patent owner/NDA holder could enter into an agreement that resulted in delayed resolution of the patent litigation. If the patent owner/NDA holder did not sue subsequent applicants, there would not be another court decision to act as an exclusivity trigger. The first applicant might not get a court decision for a long time and also might not market its product. Under these circumstances, no triggering events would occur and the first ANDA would block entry of subsequent ANDA applicants into the market.

The same blocking effect could occur even if the patent owner/NDA holder chose not to sue the first applicant with the paragraph IV certification, but instead entered into an agreement under which the first applicant would not market its product and trigger exclusivity. If the patent owner/NDA holder did not sue subsequent applicants, there also would not be a possibility of a favorable court decision to start the exclusivity period running.

The second alternative, proposing several regulatory modifications, was also rejected by the agency. Satisfactorily accomplishing the goal of promoting prompt entry of generic drug products into the market by inhibiting entry barriers would require many changes to the regulations. Additionally, it would impose a significant paperwork burden on applicants not present in the proposed rule.

The regulatory modifications would include provisions as follows: (1) An ANDA applicant would be required to notify the agency of a settlement agreement with a patent owner/NDA holder and whether it permitted immediate marketing of the drug

product; (2) an ANDA applicant would be required to market its drug product within 60 days of final approval or the agency would determine the exclusivity period commenced on the date of final approval; (3) the agency would determine that if the first applicant entered into an agreement with the patent owner/NDA holder under which it received a commercial benefit, the applicant had commercially marketed its drug product; and (4) if an ANDA applicant brought a declaratory judgment action against the patent owner/NDA holder that was dismissed for lack of case or controversy, the agency would determine that the court decision exclusivity trigger was satisfied.

These proposed regulatory modifications all have the advantage of limiting barriers to entry of generic drug products into the market by permitting earlier satisfaction of the exclusivity triggers in some cases. However, they also are associated with significant disadvantages. This alternative would impose a substantial paperwork burden on ANDA applicants by requiring them to notify the agency of settlements and submit documents relevant to settlement and declaratory judgment actions. Additionally, the approach would require the agency to collect and assess paperwork associated with financial agreements between an ANDA applicant and patent owner/NDA holder to determine if the applicant received a commercial benefit.

VI. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). A description of

the provisions is given below with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications.

Description: FDA regulations at § 314.107 govern 180-day generic drug exclusivity under the act. This proposed rule would revise § 314.107 to clarify and modify eligibility requirements for ANDA applicants seeking 180-day marketing exclusivity for a generic drug product. This new approach is necessary because of recent court decisions rejecting the previous requirement that an ANDA applicant successfully defend against a patent infringement lawsuit before it is eligible for exclusivity.

Under proposed § 314.107(e), if the first ANDA applicant for which 180-day exclusivity has started wants to waive its exclusivity in favor of a subsequent

ANDA applicant, it must so notify the agency in writing before the agency would approve the subsequent application. The first applicant would be required to notify the agency as to which subsequent applicant(s) it wants to waive the exclusivity in favor of and the effective date(s) of the waiver.

The only new information collection requirement in this proposed rule is in § 314.107(e). The industry burden for all other information collection requirements under these regulations has been estimated by FDA and approved under OMB Control Numbers 0910-0001 (approval expires November 30, 2001) and 0910-0305 (approval expires May 31, 2001).

Description of Respondents: Business or other for-profit organizations.

In 1997, 431 generic drug product approvals (including different product strengths) were distributed among 96 pharmaceutical companies. The 64 applications that became first generic approvals for a specific brand name drug, however, were submitted by only 30 firms. Moreover, the 14 first generic approvals that included a paragraph IV certification were submitted by only 5 firms. Based on this data concerning the number of first generic approvals with paragraph IV certifications for a particular drug product received by the agency in 1997, FDA estimates that approximately 14 waivers may be submitted annually under proposed § 314.70(e). FDA estimates that approximately five applicants may submit such waivers and that it will take approximately 2 hours to prepare and submit each waiver to FDA. The following table indicates the estimated annual reporting burden for the preparation of notices of exclusivity waivers.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	Number of Respondents	Number of Responses Per Respondent	Total Annual Responses	Hours per Response	Total Hours
314.107(e)	5	approx. 3	14	2	28
Total					28

¹There are no capital costs associated with this collection of information.

In compliance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted a copy of this proposed rule to OMB for its review and approval of these information collections. Interested persons are requested to send comments regarding this information collection, including suggestions for reducing this burden, to the Office of Information and

Regulatory Affairs (address above). Submit written comments on the information collection by September 7, 1999.

VII. Request for Comments

Interested persons may, on or before November 4, 1999, submit to the Dockets Management Branch (address above) written comments on this

proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

VIII. Proposed Effective Date

FDA proposes that any final rule that may issue based on this proposal become effective 30 days from publication of the final rule.

IX. References

The following references are on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry*, 1998. Also available on the Congressional Budget Office web site at: "http://www.cbo.gov".

2. FDA, Internal FDA Study, 1999.

List of Subjects in 21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 314 be amended as follows:

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

1. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 371, 374, 379e.

2. In § 314.107, redesignate paragraph (e) as paragraph (f) and paragraph (f) as paragraph (h); revise paragraphs (a), (b) introductory text, (b)(3)(i), (c), (d) and newly redesignated paragraphs (f) and (h); and add new paragraphs (e) and (g) to read as follows:

§ 314.107 Effective date of approval of a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act.

(a) *General.* (1) A drug product may be introduced or delivered for introduction into interstate commerce when approval of the application or abbreviated application for the drug product becomes effective. Except as provided in this section, approval of an application or abbreviated application for a drug product becomes effective on the date FDA issues an approval letter under § 314.105 for the application or abbreviated application.

(2) *Definitions.* The following definitions of terms apply to this section:

180-day exclusivity means the 180-day period, under section 505(j)(5)(B)(iv) of the act, during which the first applicant is protected from competition of subsequent applicants.

ANDA means an abbreviated application, as defined under § 314.3.

Decision of a court refers to a final court decision finding the patent to be invalid, unenforceable, or not infringed, resulting from patent litigation brought against the first applicant or against any subsequent applicant. This includes a final court decision in a declaratory judgment action finding the patent to be invalid, unenforceable, or not infringed.

Final court decision means a final judgment from which no appeal can be or has been taken.

First applicant means the applicant submitting the first substantially complete abbreviated new drug application (ANDA) for a particular listed drug that contains "a paragraph IV certification"¹ to any patent for the listed drug submitted to FDA and published under section 505(b) of the act. The first applicant includes all applicants filing substantially complete ANDA's with paragraph IV certifications for the same drug product on the first day that the agency receives applications with a paragraph IV certification for the drug product.

NDA means a new drug application approved under section 505(c) of the act.

NDA holder means the applicant that owns an approved NDA, or its representative or exclusive licensee. An NDA holder may also be the exclusive licensee or representative of the patent owner.

Obtains a favorable court decision means either a first applicant receives a final court decision in its patent litigation that the patent is invalid, unenforceable, or not infringed; or in litigation of a subsequent applicant involving the same patent there is a final court decision that the patent is invalid, unenforceable, or not infringed.

Paragraph IV certification means a certification under section 505(j)(2)(A)(vii) of the act that a relevant patent is invalid, unenforceable, or will not be infringed.

Patent owner means the owner of the patent which is the subject of the paragraph IV certification, or the patent owner's representative or exclusive licensee.

Subsequent applicant means any applicant filing a subsequent ANDA.

Subsequent ANDA means an ANDA that contains a paragraph IV certification and refers to the same listed drug as the first substantially complete ANDA containing a paragraph IV certification.

Substantially complete means an ANDA that contains information

required by section 505(j)(2)(A) of the act and §§ 314.50 and 314.94, including the results of any required bioequivalence studies or, if applicable, a request for a waiver of such studies, and a complete statistical analysis of required bioequivalence studies demonstrating that the drug product proposed in the ANDA meets the appropriate bioequivalence standard.

A triggering event occurs when, during a triggering period, a first applicant commercially markets its drug product or obtains a favorable court decision.

Triggering period means a 180-day time period, usually beginning on the date of the tentative approval of a subsequent ANDA, during which 180-day exclusivity may begin for the first applicant if a triggering event occurs.

(b) *Effect of patent on the listed drug.* If approval of an ANDA submitted under section 505(j) of the act or of a 505(b)(2) application is granted, that approval will become effective in accordance with the following:

* * * * *

(3) *Disposition of patent litigation.* (i)(A) Except as provided in paragraphs (b)(3)(ii), (b)(3)(iii), and (b)(3)(iv) of this section, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or NDA holder brings suit for patent infringement within 45 days of receipt by the patent owner or NDA holder of the notice of certification from the applicant under § 314.52 or § 314.95, approval may be made effective 30 months after the date of the receipt of the notice of certification by the patent owner or NDA holder unless the court has extended or reduced the period because of a failure of either the plaintiff or defendant to cooperate reasonably in expediting the action; or

(B) If the patented drug product qualifies for 5 years of exclusive marketing under section § 314.108(b)(2) and the patent owner or NDA holder brings suit for patent infringement during the 1-year period beginning 4 years after the date the patented drug was approved and within 45 days of receipt by the patent owner or NDA holder of the notice of certification, the approval may be made effective at the expiration of 7 1/2 years from the date of approval of the application for the patented drug product.

* * * * *

(c) *Exclusivity and triggering period for ANDAs.* (1) Approval of a subsequent ANDA will be made effective no sooner than 180 days from

¹ As defined elsewhere in this section.

whichever of the following dates occurs first:

(i) The date the first applicant first commences commercial marketing of its drug product; or

(ii) The date of a decision of a court holding the relevant patent invalid, unenforceable, or not infringed.

(2) For purposes of paragraph (c)(1) of this section, FDA will delay the effective date of approval of a subsequent ANDA for up to 180 days from the date described in paragraph (c)(1) of this section only when the first applicant is eligible for 180-day exclusivity. FDA will not award 180-day exclusivity to any applicant if the first applicant is no longer eligible to receive 180-day exclusivity.

(3) If the patent owner or NDA holder sues the first applicant within 45 days of receipt of the first applicant's notice of paragraph IV certification under § 314.95, and the first applicant loses the patent litigation, the first applicant must amend its certification in accordance with § 314.94(a)(12)(viii)(A) within 10 working days of the court decision finding the patent infringed. The first applicant's ANDA then no longer contains a paragraph IV certification and is not eligible for 180-day exclusivity. Immediately after such an amendment, FDA may approve eligible subsequent ANDA's.

(4) The first applicant must notify FDA of the date it commences commercial marketing of its drug product. Commercial marketing commences with the first date of introduction or delivery for introduction into interstate commerce outside the control of the manufacturer of a drug product, except for investigational use under part 312 of this chapter, but does not include transfer of the drug product for reasons other than sale within the control of the manufacturer or application holder. If the first applicant does not notify FDA within 10 working days of the date on which it began commercial marketing of its drug product, FDA may regard the effective date of approval as the date of the commencement of first commercial marketing.

(5)(i) If, before the 180-day exclusivity period for the first applicant has started, a subsequent applicant receives a tentative approval letter for its drug product stating that the first applicant's eligibility for 180-day exclusivity is the only obstacle to final approval of the subsequent ANDA, the first applicant will receive the 180-day exclusivity for which it is eligible if any of the following circumstances apply:

(A) The first applicant has received approval for its drug product, and,

within 180 days from the date of the subsequent applicant's tentative approval, a triggering event occurs.

(B) The first applicant has not received approval for its drug product; and the first applicant was not sued by the patent owner or NDA holder for patent infringement; and, within 180 days from the date of the subsequent applicant's tentative approval, a triggering event occurs.

(C) The first applicant's drug product is not yet eligible for approval because the first applicant was sued by the patent owner or NDA holder for patent infringement; and, under paragraph (b)(3)(i)(A) of this section, 30 months have not elapsed since the date the patent owner or NDA holder received notice of the patent certification; and, within 180 days after the expiration of the 30 months described in paragraph (b)(3)(i)(A) of this section, a triggering event occurs.

(D) The first applicant's drug product is not yet eligible for approval because the first applicant was sued by the patent owner or NDA holder for patent infringement and a court granted a preliminary injunction, as described in paragraph (b)(3)(iv) of this section, prohibiting the first applicant from engaging in the commercial manufacture or sale of the drug product; and, within 180 days from the date the injunction expires, a triggering event occurs.

(E) The first applicant does not have a full approval for its drug product; and the first applicant was sued by the patent owner or NDA holder for patent infringement and is eligible for approval under paragraph (b)(3) of this section; and, within 180 days from the date of the subsequent applicant's tentative approval, a triggering event occurs.

(ii) If the first applicant does not begin its period of 180-day exclusivity by the end of the appropriate 180-day period (triggering period) described in paragraphs (c)(5)(i)(A) through (c)(5)(i)(E) of this section, FDA will approve otherwise eligible ANDA's for the drug product.

(d) *Delay due to § 314.108 exclusivity.* The agency will delay the effective date of the approval of an ANDA or a 505(b)(2) application if delay is required by the exclusivity provisions in § 314.108. When the effective date of an application is delayed under both this section and § 314.108, the effective date will be the later of the two dates specified under this section and § 314.108.

(e) *Waivers of exclusivity by abbreviated new drug applicants.* For purposes of paragraph (c)(1) of this section, a first applicant for which the

180-day exclusivity has started with a triggering event may waive its exclusivity to permit FDA to approve one or more subsequent ANDA's during the 180-day exclusivity period. FDA may approve a subsequent applicant's ANDA only after the first applicant notifies the agency in writing that it is waiving its 180-day exclusivity with respect to a particular subsequent applicant(s) or application(s), and identifies the effective date(s) of the waiver.

(f) *Court actions.* (1) For purposes of establishing the effective date of approval based on a court judgment, the following dates will be deemed to be the date of the final court decision on the patent issues:

(i) If the district court enters a decision that the patent is invalid, unenforceable, or not infringed, and the decision is not appealed, the date on which the right to appeal lapses;

(ii) If the district court enters a decision that the patent is invalid, unenforceable, or not infringed, and the decision is appealed, the date of the first decision or order by a higher court holding or affirming the decision of the district court that the patent is invalid, unenforceable, or not infringed;

(iii) If the district court enters a decision that the patent is infringed, and the decision is appealed, the date on which the district court enters a judgment that the patent is invalid, unenforceable, or not infringed under a mandate issued by a court of appeals; and

(iv) The date of a settlement order or consent decree signed by a Federal judge that enters final judgment and includes a finding that the patent is invalid, unenforceable, or not infringed.

(2) The applicant must submit a copy of the entry of the order or judgment to the Office of Generic Drugs (HFD-600) or to the appropriate division in the Office of Review Management (HFD-20) within 10 working days of a final judgment. The patent owner and NDA holder may also submit this information.

(g) *Effect of dismissal of litigation on 30-month stay.* If the patent litigation between the ANDA applicant and the patent owner or NDA holder described in paragraph (b)(3)(A) of this section is dismissed without a court decision on the merits of the patent claim, whether the dismissal is with or without prejudice, the agency may immediately approve the ANDA that was the subject of the litigation, if it is otherwise eligible for approval.

(h) *Computation of 45-day time clock.* (1) The 45-day clock described in paragraph (b)(3) of this section begins

on the day after the date of receipt of the applicant's notice of certification by the patent owner or NDA holder, whichever date is later. When the 45th day falls on Saturday, Sunday, or a Federal holiday, the 45th day will be the next day that is not a Saturday, Sunday, or Federal holiday.

(2) The ANDA applicant or 505(b)(2) applicant must notify FDA immediately in writing of the filing of any legal action for patent infringement filed within 45 days of receipt of the notice of certification. If FDA is not so notified by the ANDA or 505(b)(2) applicant, or by the patent owner or NDA holder, before the expiration of the 45-day time period or the completion of the agency's review of the application, whichever occurs later, approval of the ANDA or the 505(b)(2) application will be made effective immediately upon expiration of the 45 days or completion of the agency's review and approval of the application, whichever date is later. The notification to FDA of the legal action must include the information in paragraphs (h)(2)(i) through (h)(2)(iv) of this section and be submitted according to paragraph (h)(2)(v) of this section as follows:

(i) The ANDA or 505(b)(2) application number;

(ii) The name of the applicant;

(iii) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and the dosage form;

(iv) A certification that an action for patent infringement, identified by number, has been filed in an appropriate court on a specified date; and

(v) An ANDA applicant must notify FDA's Office of Generic Drugs (HFD-600). A 505(b)(2) applicant must notify the appropriate review division in the Center for Drug Evaluation and Research or the Office of Generic Drugs if it is reviewing the application. A patent owner or NDA holder may also notify FDA of the filing of any legal action for patent infringement.

(3) If the patent owner or NDA holder waives its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or NDA holder submits to FDA a valid waiver before the 45 days elapse, approval of the ANDA or the 505(b)(2) application will be made effective upon completion of the agency's review and approval of the application. FDA will only accept a waiver in the following form:

(Name of patent owner or NDA holder) has received notice from (name of applicant)

under (section 505(b)(3) or (j)(2)(B) of the act) and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapses). (Name of patent owner or NDA holder) waives the opportunity provided by (section 505(c)(3)(C) or (j)(B)(2)(iii) of the act) and does not object to FDA's approval of (name of applicant)'s (505(b)(2) or ANDA) for (name of drug) with an immediate effective date on or after the date of this letter.

Dated: July 29, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99-20353 Filed 8-5-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF THE INTERIOR

Office of Surface Mining Reclamation and Enforcement

30 CFR Part 935

[OH-264-FOR]

Ohio Regulatory Program

AGENCY: Office of Surface Mining Reclamation and Enforcement (OSM), Interior.

ACTION: Proposed rule; reopening of public comment period.

SUMMARY: OSM is reopening the public comment period on a proposed amendment to the Ohio regulatory program (Ohio program) under the surface Mining Control and Reclamation Act of 1977 (SMCRA). Ohio is proposing revisions to Section 1501:13-1-04 of the Ohio Administrative Code (OAC) as it relates to exemptions for coal extraction incidental to government-financed highway or other construction. The amendment is intended to revise the Ohio program to include counterparts to the recently promulgated "AML Enhancement Rule," which revised the Federal regulations as 30 CFR 707.5 and added a new provision, at 30 CFR 874.17.

DATES: Written comments must be received by 4:00 p.m., [E.S.T.], August 23, 1999.

ADDRESSES: Mail or hand-deliver your written comments and requests to speak at the hearing to George Rieger, Field Branch Chief, at the address listed below.

You may review copies of the Ohio program, the proposed amendment, and all written comments received in response to this document at the addresses listed below during normal business hours, Monday through Friday, excluding holidays. You may receive one free copy of the proposed

amendment by contacting OSM's Appalachian Regional Coordinating Center.

George Rieger, Field Branch Chief, Appalachian Regional Coordinating Center, Office of Surface Mining Reclamation and Enforcement, 3 Parkway Center, Pittsburgh PA 15220, Telephone: (412) 937-2153.

Ohio Division of Mines and Reclamation, 1855 Fountain Square Court, Columbus, Ohio 43244, Telephone: (614) 265-1076.

FOR FURTHER INFORMATION CONTACT: George Rieger, Field Branch Chief, Appalachian Regional Coordinating Center, Telephone: (412) 937-2153. Internet: grieger@osmre.gov.

SUPPLEMENTARY INFORMATION:

I. Background on the Ohio Program

On August 16, 1982, the Secretary of the Interior conditionally approved the Ohio program. You can find background information on the Ohio program, including the Secretary's findings, the disposition of comments, and the conditions of approval in the August 10, 1982, **Federal Register** (47 FR 34688). You can find later actions on conditions of approval and program amendments at 30 CFR 935.11, 935.15, and 935.16.

II. Description of the Proposed Amendment

By letter dated March 16, 1999 (Administrative Record No. OH-2178-00) Ohio submitted a proposed amendment to its program concerning exemptions for coal extraction incidental to government-financed highway or other construction. Ohio submitted the proposed amendment at its own initiative, in order to incorporate into its program the expanded exemption recently promulgated in the Federal regulations at 30 CFR 707.5, as part of the "AML Enhancement Rule." Under this rule, approved Title IV abandoned mine land (AML) projects under SMCRA which involve incidental coal extraction and are less than 50 percent government financed may qualify for exemption. Projects which qualify for this expanded exemption must also meet the newly promulgated requirements contained in 30 CFR 874.17. (64 FR 7470, February 12, 1999). The proposed amendment was announced in the April 16, 1999, **Federal Register** (64 FR 18857). The initial comment period closed on May 17, 1999.

By letter dated July 9, 1999 (Administrative Record No. OH-2178-06) Ohio submitted a revised and final version of the proposed amendment. Ohio made this more recent submittal in