

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 314

[Docket No. 02N-0417]

RIN 0910-AC48

Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its patent submission and listing requirements for new drug applications (NDAs). The final rule clarifies the types of patents that must and must not be submitted and revises the declaration that NDA applicants must provide regarding their patents to help ensure that NDA applicants submit only appropriate patents. The final rule also revises the regulations regarding the effective date of approval for certain abbreviated new drug applications (ANDAs) and certain other new drug applications, known as 505(b)(2) applications, submitted under the Federal Food, Drug, and Cosmetic Act (the act). In certain situations, Federal law bars FDA from making the approval of certain ANDA and 505(b)(2) applications effective for 30 months if the applicant has certified that the patent claiming a drug is invalid or will not be infringed, and the patent owner or NDA holder then brings suit for patent infringement. The final rule also states that there is only one opportunity for a 30-month stay in the approval date of each ANDA and 505(b)(2) application. The final rule will make the patent submission and listing process more efficient as well as enhance the ANDA and 505(b)(2) application approval processes.

DATES: *Effective Date:* This final rule is effective on August 18, 2003.

Compliance Date: The compliance date is December 18, 2003, for the submission of information on polymorph patents.

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SUPPLEMENTARY INFORMATION:

I. Introduction

This final rule revises implementing regulations in part 314 (21 CFR part 314) for certain statutory amendments to the act, 21 U.S.C. 301 *et seq.*, relating to new drug applications and generic drug approvals. The statutory provisions were added to the act through the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417 (21 U.S.C. 355, 360cc; 35 U.S.C. 156, 271, 282) ("Hatch-Waxman Amendments"). These statutory provisions reflect an attempt to balance two competing interests: Promoting competition between "brand-name" or "innovator drugs" and "generic" drugs, and encouraging research and innovation. The act promotes competition by creating a process to expedite the filing and approval of ANDA and 505(b)(2) drug applications (applications submitted under the provisions of section 505(b)(2) of the act) and for resolving challenges to patents in court before marketing begins. At the same time, the act encourages research and innovation by protecting the patent interests of the patent owner and innovator drug company.

The final rule maintains a balance between the innovator companies' intellectual property rights and the desire to get generic drugs on the market in a timely fashion. The final rule limits to one per ANDA or 505(b)(2) application the maximum number of statutory 30-month stays of approval to which an innovator will be entitled when it submits multiple patents for the same NDA. Eliminating multiple 30-month stays will speed up the approval and market entry of generic drugs. The final rule also clarifies patent submission and listing requirements, which will reduce confusion and help curb attempts to take advantage of this process. Specifically, patents claiming packaging, intermediates, or metabolites must not be submitted for listing. Patents claiming a different polymorphic form of the active ingredient described in the NDA must be submitted if the NDA holder has test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA.

A. What Are the Statutory Provisions Which Affect Patent Submissions and the Approval of New Drugs?

To explain why we (FDA) issued the proposal, we first describe how Federal law requires NDA applicants to file patent information and how that patent

information can affect the approval of ANDA and 505(b)(2) applications. (We will refer to these as "ANDA and 505(b)(2) applicants" or "ANDA or 505(b)(2) applicants" and refer to their applications as "ANDA and 505(b)(2) applications" or "ANDA or 505(b)(2) applications" throughout the remainder of the preamble of this document.)

Section 505(b)(1) of the act (21 U.S.C. 355(b)(1)) requires all NDA applicants to file, as part of the NDA, "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." Section 505(c)(2) of the act (21 U.S.C. 355(c)(2)) imposes a similar patent submission obligation on holders of approved NDAs when the NDA holder could not have submitted the patent information with its application.

Under section 505(b)(1) of the act, we publish patent information after approval of an NDA application in our approved drug products list entitled "Approved Drug Products With Therapeutic Equivalence Evaluations." This list is known popularly as the "Orange Book" because of its orange-colored cover. If patent information is submitted after NDA approval, section 505(c)(2) of the act directs us to publish the information upon its submission.

The act also requires ANDA or 505(b)(2) applicants to make certifications regarding each of the listed patents pertaining to the drug they intend to reference (see sections 505(b)(2)(A)(i) through (b)(2)(A)(iv) and 505(j)(2)(A)(vii)(I) through (j)(2)(A)(vii)(IV) of the act (21 U.S.C. 355(b)(2)(A)(i) through (b)(2)(A)(iv) and 21 U.S.C. 355(j)(2)(A)(vii)(I) through (j)(2)(A)(vii)(IV)). In brief, these certifications state that:

- Patent information has not been filed,
- The patent has expired,
- The patent will expire on a specific date, or
- The patent is invalid or will not be infringed.

If the ANDA or 505(b)(2) applicant certifies that the patent is invalid or will not be infringed (a certification known as a "paragraph IV" certification because it is the fourth type of patent certification described in the act¹), the act requires the applicant to notify the

¹ Paragraph IV throughout also refers to paragraph iv, the comparable provision in section 505(b)(2)(A) of the act.