DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00D–1537]

Draft Guidance for Industry on Referencing Discontinued Labeling for Listed Drugs in Abbreviated New Drug Applications; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Referencing Discontinued Labeling for Listed Drugs in Abbreviated New Drug Applications.'' This document is intended to provide guidance to applicants on referencing discontinued labeling for listed drugs in abbreviated new drug applications (ANDA's) submitted for approval under the Federal Food, Drug, and Cosmetic Act (the act). This issue has only recently arisen and is not addressed directly in the agency's regulations governing the approvals of ANDA's.

DATES: Submit written comments on the draft guidance by January 24, 2001. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of this draft guidance for industry are available on the Internet at http://www.fda.gov/cder/guidance/index.htm. Submit written requests for single copies of this draft guidance to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Cecelia M. Parise, Center for Drug Evaluation and Research (HFD–600), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–5845.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman amendments) established the generic drug approval program used today to ensure that lower price generic drugs are made available to the public promptly upon the expiration of patent and exclusivity protections covering the innovator products. The generic drug approval process generally depends on the ANDA applicant establishing that the generic drug is the same as an approved innovator product (the listed drug) with respect to active ingredients, dosage form, strength, route of administration, conditions of use, and labeling.

During the period when an innovator drug is being marketed, it may undergo a number of changes that are approved through supplements to new drug applications (NDA's). Such changes can include the addition of new indications, changes to the product formulation, and labeling changes. In the past, when ANDA's have been submitted, they have referenced only the innovator drug product labeling as it appeared at the time of ANDA submission. However, recently a question has been raised as to whether, in certain circumstances, an ANDA can refer to discontinued labeling for the listed drug. The issue of referencing discontinued labeling arises when the sponsor of the listed drug product has obtained exclusivity or patent protection for a new part of product labeling and has removed a part of the previous labeling, unprotected by exclusivity or patents, for reasons other than safety or effectiveness. When the holder of the listed drug obtains approval and market protection for a change to the drug and removes the corresponding unprotected information from the current labeling, there remains no current labeling for the ANDA applicant to reference. This raises the question of whether applicants will be barred from obtaining approval for any ANDA referencing that listed drug until the protection for the particular aspect of the labeling expires, because relevant labeling is either protected or has been removed from the currently marketed product.

FDA has developed an approach to this situation that ensures that labeling removed from a drug product for reasons of safety or effectiveness cannot be referenced in an ANDA, while at the same time permitting approval of generic drugs that reference discontinued labeling for safe and effective innovator products. This approach ensures that safe and effective generic drug products are made available to the public as promptly as possible when relevant market protections have expired.

An ANDA will be permitted to reference discontinued labeling for a listed drug when: (1) The holder of the NDA for the innovator drug has obtained approval for a change in the drug labeling; (2) the change has received either a patent listed in ''Approved Drug Products with Therapeutic Equivalence Evaluations'' (the Orange Book) or market exclusivity under the act; (3) the NDA sponsor has removed or revised the labeling describing the corresponding unprotected aspects of the drug; (4) the change to the drug product is not one for which a suitability petition may be filed (21 CFR 314.93); (5) the sponsor wishing to reference the discontinued labeling has submitted a petition requesting that the agency determine whether the previous labeling was withdrawn for reasons of safety or effectiveness, or the agency on its own initiative, begins the process of determining the reasons for the withdrawal of the previous labeling; (6) the agency has determined that the previous innovator labeling was not withdrawn for reasons of safety or effectiveness; and (7) the agency has determined that omission of the protected information will not render the drug product less safe or effective than the currently marketed innovator product.

The draft guidance identifies the provisions of the act and FDA regulations relevant to this issue, and provides a detailed description of the process an ANDA applicant should follow to refer to discontinued labeling for a listed drug. It also describes the actions FDA will take to determine whether the use of such labeling is acceptable because the labeling was not withdrawn from the market for reasons of safety or effectiveness.

This draft guidance is being issued consistent with FDA's good guidance practices (65 FR 56468, September 19, 2000). The draft guidance represents the agency's current thinking on referencing discontinued labeling for listed drugs in ANDA's. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the draft guidance. 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. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: October 13, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–27452 Filed 10–25–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98D–0282]

Revised Guidance for Industry on Submitting and Reviewing Complete Responses to Clinical Holds; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised guidance for industry entitled ''Submitting and Reviewing Complete Responses to Clinical Holds.'' This guidance describes how to submit a complete response if an investigational new drug (IND) application is placed on clinical hold. The revised guidance reflects amendments to FDA's clinical hold regulations, includes the definition of a commercial IND, and discusses the agency's policy on resolving clinical trial issues that are not related to the imposition of a clinical hold.

DATES: Comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of this guidance for industry are available on the Internet at http://www.fda.gov/cder/guidance/index.htm; or http://www.fda.gov/cber/guidelines.htm. Submit written comments on this guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments are to be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Linda S. Carter (HFD–101), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–6578; or Robert A. Yetter (HFM–10), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–0373.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a revised guidance for industry entitled ''Submitting and Reviewing Complete Responses to Clinical Holds.'' Section 117 of the Food and Drug Administration Modernization Act of 1997 (Modernization Act), signed into law by President Clinton on November 21, 1997, provides that a written request that a clinical hold be removed shall receive a decision in writing, specifying the reasons for that decision, within 30 days after receipt of such request. Section 117(3)(c) of the Modernization Act is codified in the Federal Food, Drug, and Cosmetic Act at section 505(i)(3)(c) (21 U.S.C. 355(i)(3)(c)). In addition, the agency committed to user fee performance goals incorporating the same response time. In the **Federal Register** of December 14, 1998 (63 FR 68676), FDA amended its clinical hold regulations in § 312.42(e) (21 CFR 312.42(e)) to include this 30-day response requirement. This guidance describes how sponsors should submit responses to clinical holds so that they may be identified as complete responses and the agency can track the time to response.

In the **Federal Register** of May 14, 1998 (63 FR 26809), FDA published a notice announcing the availability of the original guidance and soliciting comments. Two comments on the guidance were submitted to the docket. After considering the comments, FDA is issuing a revised guidance.

The revised guidance: (1) Reflects amendments to FDA's clinical hold regulations, stating that FDA will respond in writing within 30-calendar days of receipt of a sponsor's request to release a clinical hold and complete response to the issue(s) that led to the clinical hold (§ 312.42(e)); (2) includes the definition of a commercial IND and clarifies that the Prescription Drug User Fee Act goals apply only to commercial IND's, although the 30-calendar day response applies to all IND clinical hold complete responses; and (3) states that clinical trial issues that are not related to the imposition of a clinical hold may be discussed in the letter placing the trial on clinical hold, but will be clearly marked as nonhold issues and that a sponsor's response to such nonhold issues should be addressed in a separate amendment to the IND.

The collection of information contained in the revised guidance has been approved by the Office of Management and Budget under OMB control number 0910–0445.

This revised guidance document supersedes the original guidance. This Level 1 guidance document is being issued consistent with FDA's good guidance practices (65 FR 56468, September 19, 2000). The revised guidance represents the agency's current thinking on the submission of responses to clinical holds. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the guidance at any time. 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. The guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: October 13, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–27453 Filed 10–25–00; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[Document Identifier: HCFA–304 and 304a]

Agency Information Collection Activities: Proposed Collection; Comment Request

AGENCY: Health Care Financing Administration, HHS.

In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Health Care Financing Administration (HCFA), Department of Health and Human Services, is publishing the following summary of proposed collections for public comment. Interested persons are invited to send comments regarding this burden estimate or any other aspect of this collection of information, including any of the following subjects: (1) The necessity and utility of the proposed information collection for the proper performance of the agency's functions; (2) the accuracy of the estimated burden; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) the use of automated collection techniques or other forms of information technology to minimize the information collection burden.

Type of Information Collection Request: Extension of a currently approved collection; *Title of Information Collection:* Reconciliation