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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99D-1149]

Draft Guidance for Industry on in Vivo Pharmacokinetics and Bioavailability Studies and in Vitro Dissolution Testing for Levothyroxine Sodium Tablets; Availability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SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "In Vivo Pharmacokinetics and Bioavailability Studies and in Vitro Dissolution Testing for Levothyroxine Sodium Tablets." The draft guidance contains agency recommendations on how to design in vivo pharmacokinetics and bioavailability studies and perform in vitro dissolution testing for levothyroxine sodium tablets.

DATES: Written comments on the draft guidance may be submitted by (*insert date 60 days after date of publication in the Federal Register*). General comments on documents are welcome at any time.

ADDRESSES: Copies of this draft guidance for industry can be obtained on the Internet at "<http://www.fda.gov/cder/guidance/index.htm>". Submit written requests for single copies of the draft guidance to the Drug Information Branch (HFD-210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.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 Submit written comments on the draft guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments and requests are to be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Michael J. Fossler, Center for Drug Evaluation and Research (HFD-870), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6417.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance for industry entitled “In Vivo Pharmacokinetics and Bioavailability Studies and in Vitro Dissolution Testing for Levothyroxine Sodium Tablets.” This draft guidance contains agency recommendations on how to design in vivo pharmacokinetics and bioavailability studies and perform in vitro dissolution testing for levothyroxine sodium tablets, which were identified as new drugs in a notice published in the **Federal Register** of August 14, 1997 (62 FR 43536).

Levothyroxine sodium was introduced into interstate commerce during the 1950’s without approval of new drug applications (NDA’s) for the drug products. As a result of concerns about the stability and consistent potency of the products, the agency announced that orally administered drug products containing levothyroxine sodium were new drugs (62 FR 43536). The notice stated that a manufacturer who wished to continue to market orally administered levothyroxine sodium products had to submit an NDA. The agency allowed current manufacturers 3 years to obtain approved NDA’s, until August 14, 2000.

A number of firms have contacted FDA for advice regarding how to conduct bioavailability studies and in vitro dissolution testing for levothyroxine sodium tablets. Because of this interest, and the need to provide consistent advice to all firms who intend to submit NDA’s for this product, FDA has developed this draft guidance on designing in vivo pharmacokinetics and bioavailability studies and performing in vitro dissolution testing for levothyroxine sodium tablets. The guidance documents FDA’s current thinking on this subject. Although the guidance is being submitted in draft for comment, FDA recognizes that sponsors of already marketed levothyroxine sodium products that are required to obtain approved NDA’s by August 14, 2000, may already have begun to conduct bioavailability and dissolution studies. The study design described in this guidance may be used for these studies or an alternative approach may be used. In either case, the study designs

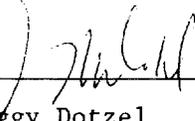
will be acceptable if scientifically justified. FDA will revise the study designs described in the guidance in accordance with any comments received, if appropriate.

This level 1 draft guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). The draft guidance represents the agency's current thinking on in vivo pharmacokinetics and bioavailability studies and in vitro dissolution testing for levothyroxine sodium tablets. 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, regulations, or both.

Interested persons may, on or before (*insert date 60 days after date of publication in the Federal Register*), 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 may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: Jun 3, 1999
June 3, 1999



Peggy Dotzel
Acting Associate Commissioner for
Policy Coordination

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL



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