

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 97N-0314]

DMB

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**Guidance for Industry on Levothyroxine Sodium Products—Enforcement of August 14, 2001, Compliance Date and Submission of New Applications; Availability**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Levothyroxine Sodium Products—Enforcement of August 14, 2001, Compliance Date and Submission of New Applications.” This guidance discusses how FDA plans to exercise its enforcement discretion after August 14, 2001, with regard to levothyroxine sodium products that are marketed without approved applications. This guidance also answers certain frequently asked questions concerning the submission of applications for levothyroxine sodium products. It replaces the previously issued guidance entitled “Levothyroxine Sodium, Questions and Answers” (February 2001).

**DATES:** Submit written or electronic comments on agency guidances at any time.

**ADDRESSES:** Submit written requests for single copies of this guidance to the Division of Drug Information (HFD-240), 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 guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

**FOR FURTHER INFORMATION CONTACT:** David T. Read, 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**

FDA is announcing the availability of a guidance for industry entitled "Levothyroxine Sodium Products—Enforcement of August 14, 2001 Compliance Date and Submission of New Applications." This guidance discusses how FDA plans to exercise its enforcement discretion after August 14, 2001, with regard to levothyroxine sodium products that are marketed without approved applications. This guidance also answers certain frequently asked questions concerning the submission of applications for levothyroxine sodium products and replaces the previously issued guidance entitled "Levothyroxine Sodium, Questions and Answers" (February 2001) (see 66 FR 13935, March 8, 2001).

In the **Federal Register** of August 14, 1997 (62 FR 43535), FDA announced that orally administered levothyroxine sodium drug products are new drugs. The notice stated that by August 14, 2000, manufacturers who wish to continue to market these products must obtain approved applications as required by section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) and 21 CFR part 314. The notice stated that after August 14, 2000, any orally administered drug product containing levothyroxine sodium that is introduced or delivered for introduction into interstate commerce without an approved application will be subject to regulatory action, unless found by FDA to be not subject to the new drug requirements of the act under a citizen petition submitted for that product. FDA issued a second **Federal Register** notice on April 26, 2000 (65 FR 24488), extending the deadline for obtaining approved applications until August 14, 2001.

The agency permitted orally administered levothyroxine sodium products to remain on the market during this period of time without approved new drug applications to give manufacturers

time to conduct the required studies, prepare applications, and have them approved. FDA stated in the 1997 **Federal Register** notice that levothyroxine sodium products are used to treat hypothyroidism, and no alternative drug is relied on by the medical community as an adequate substitute.

As of June 2001, two orally administered levothyroxine sodium products have been approved by FDA. These approved products have been evaluated by FDA and found to be safe and effective for their intended uses. FDA has not evaluated the safety and effectiveness of unapproved marketed products, but it has determined that no currently marketed unapproved orally-administered levothyroxine sodium product is generally recognized as safe and effective (see 62 FR 43535 at 43538, August 14, 1997).

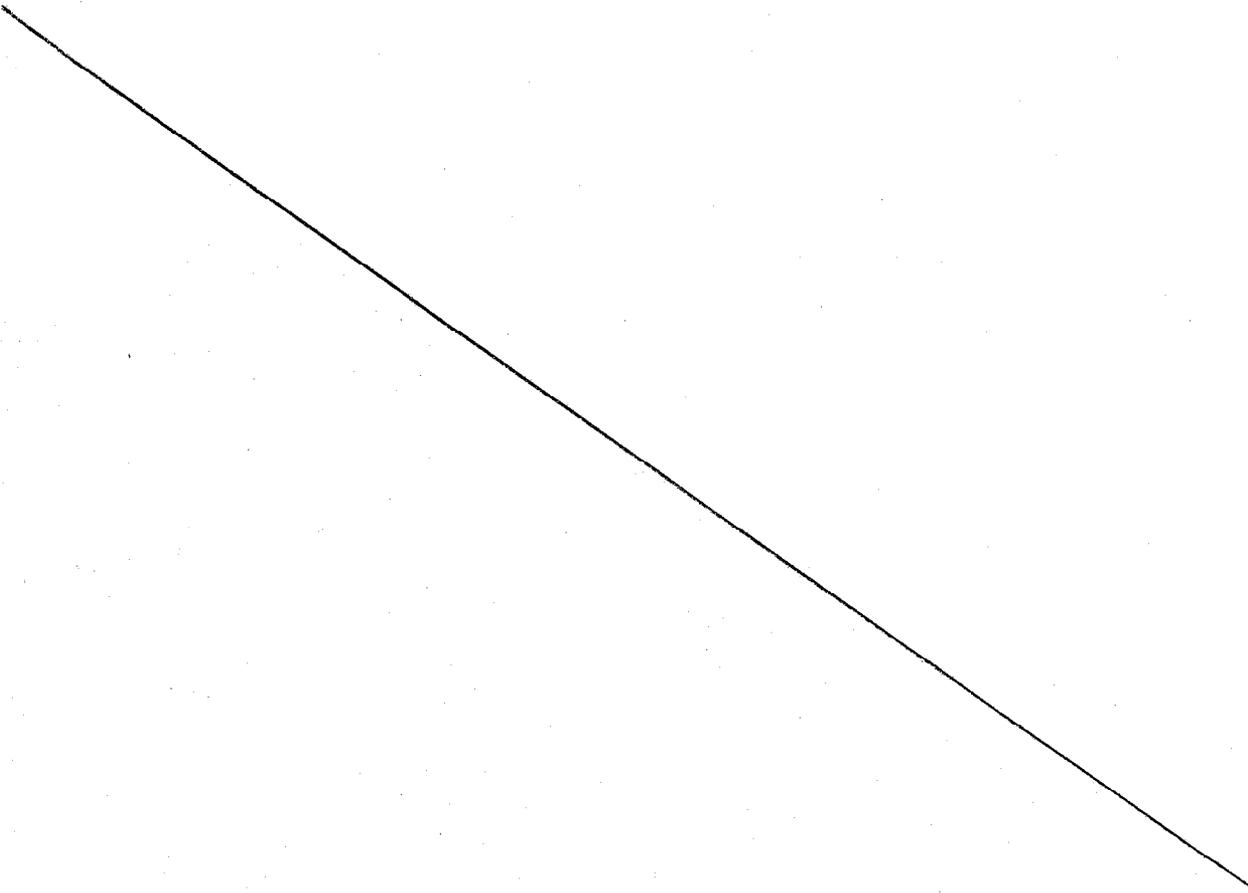
Notwithstanding the fact that there are now two approved applications for orally administered levothyroxine sodium, FDA has determined that it will take time for the millions of patients taking unapproved products to switch to approved products, and for manufacturers of approved products to scale up their production and to introduce this increased production into the distribution chain. To provide time for manufacturers of approved products to scale up their production and for patients and health care providers to make a reasonable transition from unapproved to approved products, FDA has decided to continue to exercise its enforcement discretion by establishing a gradual phase-out of unapproved products. The phase-out plan and a number of frequently asked questions are addressed in this guidance.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115; 65 FR 56468, September 19, 2000). The guidance is being implemented immediately without prior public comment because there are public health reasons for the immediate implementation of the guidance document. The guidance pertains to the agency's exercise of enforcement discretion and it is being issued to facilitate planning by patients, health care providers, manufacturers, and distributors who need information about the agency's plans to transition patients from unapproved to approved levothyroxine sodium products after August 14, 2001. The guidance

represents the agency's current thinking on this topic. 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.

## **II. Comments**

Interested persons may, at any time, submit written or electronic comments on the guidance to the Dockets Management Branch (address above). 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.

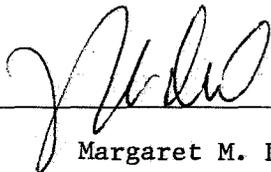


**III. Electronic Access**

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

Dated: 7-9-01

July 9, 2001.



Margaret M. Dotzel,  
Associate Commissioner for Policy.

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