

## VII. Legal Status

Levothyroxine sodium is used as replacement therapy when endogenous thyroid hormone production is deficient. The maintenance dosage must be determined on a patient-by-patient basis. Levothyroxine sodium products are marketed in multiple dosage strengths, that may vary by only 12 micrograms, thus permitting careful titration of dose. Because of levothyroxine sodium's narrow therapeutic index, it is particularly important that the amount of available active drug be consistent for a given tablet strength.

Variations in the amount of available active drug can affect both safety and effectiveness. Patients who receive superpotent tablets may experience angina, tachycardia, or arrhythmias. There is also evidence that overtreatment can cause osteoporosis. Subpotent tablets will not be effective in controlling hypothyroid symptoms or sequelae.

The drug substance levothyroxine sodium is unstable in the presence of light, temperature, air, and humidity. Unless the manufacturing process can be carefully and consistently controlled, orally administered levothyroxine sodium products may not be fully potent through the labeled expiration date, or be of consistent potency from lot to lot.

There is evidence from recalls, adverse drug experience reports, and inspection reports that even when a physician consistently prescribes the same brand of orally administered levothyroxine sodium, patients may receive products of variable potency at a given dose. Such variations in product potency present actual safety and effectiveness concerns.

In conclusion, the active ingredient levothyroxine sodium is effective in treating hypothyroidism and is safe when carefully and consistently manufactured and stored, and prescribed in the correct amount to replace the deficiency of thyroid hormone in a particular patient. However, no currently marketed orally administered levothyroxine sodium product has been shown to demonstrate consistent potency and stability and, thus, no currently marketed orally administered levothyroxine sodium product is generally recognized as safe and effective. Accordingly, any orally administered drug product containing levothyroxine sodium is a new drug under section 201(p) of the act (21 U.S.C. 321(p)) and is subject to the requirements of section 505 of the act.

Manufacturers who wish to continue to market orally administered levothyroxine sodium products must submit applications as required by section 505 of the act and part 314 (21 CFR part 314). FDA is prepared to accept NDA's for these products, including section 505(b)(2) applications. An applicant making a submission under section 505(b)(2) of the act may rely upon investigations described in section 505(b)(1)(A) that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. For example, such an application may include literature supporting the safety and/or the effectiveness of levothyroxine sodium. A bioavailability study must be completed and submitted as part of an NDA, including a 505(b)(2) application, in order to evaluate the safety and efficacy of these products.

If the manufacturer of an orally administered drug product containing levothyroxine sodium contends that the drug product is not subject to the new drug requirements of the act, this claim should be submitted in the form of a citizen petition under § 10.30 and should be filed to Docket No. 97N-0314 no later than October 14, 1997. Sixty days is the time allowed for such submissions in similar proceedings. (See § 314.200(c) and (e).) Under § 10.30(e)(2), the agency will provide a response to each petitioner within 180 days of receipt of the petition. A citizen petition that contends that a particular drug product is not subject to the new drug requirements of the act should contain the quality and quantity of data and information set forth in § 314.200(e). Note especially that a contention that a drug product is generally recognized as safe and effective within the meaning of section 201(p) of the act is to be supported by the same quantity and quality of scientific evidence that is required to obtain approval of an application for the product. (See § 314.200(e)(1).)

Levothyroxine sodium products are medically necessary because they are used to treat hypothyroidism and no alternative drug is relied upon by the medical community as an adequate substitute. Accordingly, FDA will permit orally administered levothyroxine sodium products to be marketed without approved NDA's until August 14, 2000, in order to give manufacturers time to conduct the required studies and to prepare and submit applications, and to allow time for review of and action on these applications. This provision for

continuation of marketing, which applies only to levothyroxine sodium products marketed on or before the publication of this notice, is consistent with the order in *Hoffmann-La Roche, Inc. v. Weinberger*, 425 F. Supp. 890 (D.D.C. 1975), reprinted in the **Federal Register** of September 22, 1975 (40 FR 43531) and March 2, 1976 (41 FR 9001).

After August 14, 2000 any orally administered drug product containing levothyroxine sodium, marketed on or before the date of this notice, that is introduced or delivered for introduction into interstate commerce without an approved application will be subject to regulatory action, unless there has been a finding by FDA, under a citizen petition submitted for that product as described above, that the product is not subject to the new drug requirements of the act.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505 (21 U.S.C. 352, 355)) and under authority delegated to the Deputy Commissioner for Policy (21 CFR 5.20).

Dated: August 7, 1997.

**William K. Hubbard,**  
Associate Commissioner for Policy  
Coordination.

[FR Doc. 97-21575 Filed 8-13-97; 8:45 am]

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### National Consumer Forum; Notice of Meeting

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

**ACTION:** Notice of meeting.

**SUMMARY:** The Food and Drug Administration (FDA), Office of Consumer Affairs (OCA), is announcing the first in a series of National Consumer Forums. These forums are an opportunity to engage in open dialog with consumers on health issues and agency actions.

**DATES:** The meeting will be held on Tuesday, September 23, 1997, from 1 p.m. to 3 p.m. Due to space limitations, preregistration is recommended.

**ADDRESSES:** The meeting will be held in the Truman Room of the White House Conference Center, 726 Jackson Pl. NW., Washington, DC 20006. Use Metro Stop Farragut North, K Street Exit on the Red Line, and Farragut West on Blue/Orange Line.

**FOR FURTHER INFORMATION CONTACT:** Carol M. Lewis, Office of Consumer

Affairs (HFE-1), Food and Drug Administration, Parklawn Bldg., 5600 Fishers Lane, rm. 16-85, Rockville, MD 20857, 301-827-4404, FAX 301-827-3052, or e-mail "clewis@bangate.fda.gov".

**SUPPLEMENTARY INFORMATION:** The purpose of this meeting is to provide an opportunity for consumers to discuss their concerns and thereby participate in agency decision and policymaking on key health care and consumer protection issues. To register for the meeting and obtain directions, please call, fax, or e-mail the contact person (address above). Include the name, title, telephone and fax numbers of the person attending, and the name of the organization being represented.

If special accommodations are required due to a disability, please contact Carol M. Lewis at least 7 days in advance of the meeting.

Dated: August 8, 1997.

**William K. Hubbard,**

*Associate Commissioner for Policy Coordination.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### Advisory Committee; Notice of Meeting

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

**ACTION:** Notice.

This notice announces a forthcoming meeting of public advisory committees of the Food and Drug Administration (FDA). The meeting will be open to the public.

*Name of Committees:* Joint meeting of the Nonprescription Drugs Advisory Committee and Pulmonary-Allergy Drugs Advisory Committee.

*General Function of the Committees:* To provide advice and recommendations to the agency on FDA regulatory issues.

*Date and Time:* The meeting will be held on September 19, 1997, 8:30 a.m. to 5 p.m.

*Location:* Holiday Inn, Ballroom, Two Montgomery Village Ave., Gaithersburg, MD.

*Contact Person:* Andrea G. Neal or Leander B. Madoo, Center for Drug Evaluation and Research (HFD-21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5455, or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the

Washington, DC area), codes 12541 and 12545. Please call the Information Line for up-to-date information on this meeting.

*Agenda:* The committees will jointly consider new drug application (NDA) 20-840, Beconase® Allergy Nasal Spray (belcomethasone dipropionate 0.042%, monohydrate, Glaxo Wellcome, Inc.) for over-the-counter treatment and prevention of the symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

*Procedure:* Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by September 5, 1997. Oral presentations from the public will be scheduled between approximately 8:30 a.m. to 9:30 a.m. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before September 5, 1997, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: August 7, 1997.

**William B. Schultz,**

*Acting Lead Deputy Commissioner for the Food and Drug Administration.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### Advisory Committee; Notice of Meeting

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

**ACTION:** Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

*Name of Committee:* Nonprescription Drugs Advisory Committee.

*General Function of the Committee:* To provide advice and recommendations to the agency on FDA regulatory issues.

*Date and Time:* The meeting will be held on September 18, 1997, from 8:30 a.m. to approximately 5 p.m.

*Location:* Holiday Inn, The Ballroom, Two Montgomery Village Ave., Gaithersburg, MD.

*Contact Person:* Andrea G. Neal, Center for Drug Evaluation and Research (HFD-21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5455, or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area), code 12541. Please call the Information Line for up-to-date information on this meeting.

*Agenda:* The Committee will discuss issues relating to the labeling and dosing of over-the-counter (OTC) pediatric analgesic/antipyretic drug products. The Committee will discuss topics such as: (1) What is an appropriate lower age limit for the dosing of OTC analgesic/antipyretic drug products; and (2) the safety implications of the OTC availability of children's analgesic/antipyretic suspension products and double concentrated infant drops with overlapping age directions.

*Procedure:* Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Written submissions may be made to the contact person by September 12, 1997. Oral presentations from the public will be scheduled between approximately 1 p.m. and 2 p.m. Time allotted for each presentation may be limited. Those desiring to make formal oral presentations should notify the contact person before September 12, 1997, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation.

Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C., app. 2).

Dated: August 7, 1997.

**William B. Schultz,**

*Acting Lead Deputy Commissioner for the Food and Drug Administration.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### Advisory Committee; Notice of Meeting

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

**ACTION:** Notice.