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March 15, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Prescription Drug Products;
Levothyroxine Sodium
Docket No. 97N-0314

In the Federal Register notice initiating this proceeding, the Food and Drug Administration invited manufacturers of levothyroxine sodium drug products who believe that their products are not new drugs to submit a citizen petition to this docket. My client, Knoll Pharmaceutical Company, submitted such a citizen petition on December 15, 1997, asserting that Synthroid brand orally administered levothyroxine sodium USP is generally recognized as safe and effective ("GRAS/E") for replacement or supplement therapy in hypothyroidism. Knoll submitted a supplement to its citizen petition on May 29, 1998, asserting that Synthroid is also generally recognized as safe and effective for use as a pituitary TSH suppressant in certain thyroid cancer indications. The citizen petition, as supplemented, has not been acted on by the agency.¹

A recent letter from FDA (copy attached) suggests that the agency may have prejudged the issue of whether Synthroid is GRAS/E. The letter says that "Levothyroxine drug products, such as . . . Synthroid, are not generally recognized as safe and effective. . ." The letter's failure to acknowledge that FDA has invited and Knoll has submitted a citizen petition to resolve this very issue, and especially the unequivocal manner in which the letter states that the product is not GRAS/E, are extremely troubling. Knoll is entitled to full and fair consideration of its citizen petition by FDA staff who are willing to consider the issues on their merits. The attached letter, however, strongly suggests that the agency has prejudged the issues and/or that the FDA staff who will review the citizen petition believe or could believe

1. As set forth in Knoll's separate Citizen Petition regarding Scheduling and Procedure, submitted to this docket on September 25, 1998, Knoll has submitted Freedom of Information Act requests the responses to which it intends to use in supplementing its GRAS/E Citizen Petition, but the agency has not yet completed its responses to these FOIA requests. Knoll has been advised by FDA staff that the company will be given sufficient time to supplement its Citizen Petition after FDA provides a complete response to Knoll's FOIA requests.

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that their colleagues and/or superiors have prejudged the issues.

Knoll therefore calls upon FDA to state in writing that the issue of whether Synthroid is a new drug has not yet been decided and that Knoll's citizen petition in this matter will receive full and fair consideration without prejudgement of the issues.

Sincerely,

A handwritten signature in black ink, appearing to read "N. L. Buc". The signature is fluid and cursive, with a long horizontal stroke at the end.

Nancy L. Buc
Counsel to
Knoll Pharmaceutical Company



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOI

Food and Drug Administration
Rockville MD 20857

FEB 1 1999

TRANSMITTED VIA FACSIMILE

Nancy Cafmeyer
Regulatory Affairs
Jones Medical Industries, Inc.
1945 Craig Road
P.O. Box 46903
St. Louis, Missouri 63146

**RE: Levoxyl (levothyroxine sodium tablets, USP)
MACMIS # 6649**

Dear Ms. Cafmeyer:

This letter addresses Jones Medical Industries, Inc.'s (Jones') dissemination of a journal advertisement for Levoxyl, entitled "Take A Closer Look," that was published in Pharmacist magazine in September 1998. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed this advertisement as part of its monitoring and surveillance program. DDMAC has concluded that Jones' advertisement is in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations.

Specifically, DDMAC objects to the statement that "Levoxyl is interchangeable with Synthroid . . ." since it suggests that Levoxyl is a levothyroxine drug product that has been determined to be bioequivalent to Synthroid by the U.S. Food and Drug Administration (FDA). Levoxyl and Synthroid are brand name levothyroxine sodium product. However, neither product has been demonstrated to FDA to be either equivalent to the other or inequivalent to the other. Thus any claims of equivalence are unsupported.

Levothyroxine drug products, such as Levoxyl and Synthroid, are not generally recognized as safe and effective and are not currently recognized by FDA as bioequivalent. No levothyroxine sodium drug product appears in the FDA Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). For more information about the legal status of these products, we refer you to 62 Fed. Reg.

43535-38 (August 14, 1997) (Prescription Drug Products; Levothyroxine Sodium).

In order to address the objections cited in this letter, DDMAC suggests that Jones take the following actions:

(1) Immediately discontinue the dissemination of this advertisement and all other promotional materials for Levoxyl bearing the same or similar violative presentations upon receipt of this letter.

(2) Provide to DDMAC, in writing, Jones' commitment to comply with number one above.

Jones' response should be received no later than February 12, 1999. If Jones has any questions or comments, please contact the undersigned or Jayne Peterson, R.Ph., J.D., by facsimile at 301-594-6771, or in writing at the Division of Drug, Marketing, advertising, and Communications, HFD-40, Room 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

In all correspondence related to this matter, please refer to MACMIS #6649.

Sincerely,

Lesley R. Frank, Ph.D., J.D.
Regulatory Counsel,
Division of Drug Marketing, Advertising,
and Communications