Dear:

The purpose of this letter is to inform you that the Food and Drug Administration (FDA) has decided to require that all levothyroxine sodium products approved for use in humans meet a 95 to 105 percent potency specification throughout their labeled shelf-lives.

This action is part of the agency's ongoing efforts to address concerns expressed about the performance of currently approved levothyroxine sodium products. It is consistent with FDA's previous regulatory actions intended to ensure that levothyroxine sodium drug products maintain their quality throughout their shelf-lives. It is based on our evaluation of data submitted as part of the drug approval process, evaluation of stability data provided by applicants in the spring of 2006, evaluation of available clinical data and literature, discussions and opinions expressed at an October 2006 joint meeting of the Endocrine and Metabolic Drugs Advisory Committee (EMDAC) and Advisory Committee for the Pharmaceutical Sciences (ACPS), and further evaluation of the joint advisory committee panel's recommendation. (See transcript of the October 4, 2006 joint meeting of the EMDAC and ACPS at http://www.fda.gov/ohrms/dockets/ac/cder06.html#.) The joint advisory committee panel voted, almost unanimously, that a 10 percent loss in potency over shelf life raises clinically significant concerns and recommended that the potency specifications for levothyroxine sodium products be narrowed from 90 to 110 percent to 95 to 105 percent.

FDA will work with the United States Pharmacopeia (USP) to change the potency specification indicated in the USP monograph for levothyroxine sodium tablets from 90 to 110 percent to 95 to 105 percent of labeled claim.

Within 18 months of the date of this letter, we request that you submit a supplement to your approved application to incorporate the 95 to 105 percent specification and to reflect any expiration date revisions that may be necessary to meet the 95 to 105 percent potency specification. Also within 18 months, if you intend to make modifications to the manufacturing process and/or the product formulation of your marketed levothyroxine sodium product to meet the revised specifications, you must submit a *Prior Approval Supplement* under 21 CFR 314.70(b) so that the agency can review and approve the proposed changes. We expect all approved products to have the revised potency specifications incorporated in their applications and meet the revised potency specifications within 24 months of the date of this letter.

If modifications to your currently marketed levothyroxine sodium product are necessary to comply with the 95 to 105 percent potency specification and you fail to make them expeditiously, FDA may deem your product to be adulterated and/or misbranded under the Federal Food, Drug, and Cosmetic Act. FDA recognizes that levothyroxine sodium is medically necessary because it is used to treat hypothyroidism and as thyroid replacement therapy, and no alternative drug is relied upon by the medical community as an adequate substitute. However, as a result of FDA's previous regulatory efforts and drug approvals, there are levothyroxine sodium products that are currently available and marketed that meet the 95-105 percent potency specification.

If you have any questions concerning this request, please contact….

Thank you for your assistance in this matter.

Sincerely,

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