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November 17, 2000

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

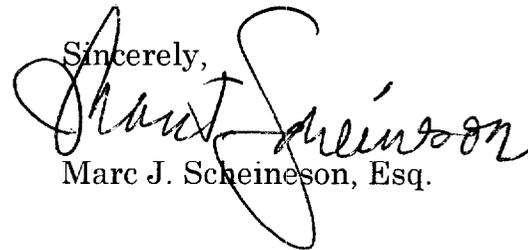
Re: Compliance Date for Approved New Drug Applications for Orally Administered
Levothyroxine Sodium Drug Products; Docket No. 97N-0314

Dear Sir or Madam:

Attached please find a citizen's petition filed on behalf of our client, Jerome Stevens Pharmaceuticals, Inc. (JSP). This petition requests that the Food and Drug Administration (FDA) refuse to extend any further the deadline for manufacturers of orally administered levothyroxine sodium drug products to obtain approved new drug applications (NDAs) as a condition for continuing to market the synthetic thyroid drug. That deadline has already been extended one full year to its current date of August 14, 2001. JSP properly filed an NDA based on the prior deadline of August 14, 2000. That NDA was approved by FDA on August 21, 2000. Therefore, there is already a FDA-approved synthetic thyroid drug on the market. JSP has the manufacturing capacity to satisfy all current demand. It faithfully complied with FDA's request for data. Therefore, others who resisted this requirement should not benefit further, to the prejudice of JSP, through any additional delay in the date an approved NDA must be in place.

We appreciate your accepting this petition for filing, and your properly considering it as part of the administrative record pursuant to 21 C.F.R. § 10.30.

Please contact me at (202) 414-9243 with your response, of if we may be of further assistance.

Sincerely,

Marc J. Scheineson, Esq.

cc: Ms. Christine F. Rogers
Mr. Ronald Steinlauf

97N-0314

1301 K Street, N.W. Delaware
Suite 1100 - East Tower New Jersey
Washington, D.C. 20005 New York
202.414.9200 Pennsylvania
Fax 202.414.9299 Virginia
Washington, DC

CP4
reedsmith.com

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Re: Compliance Date for Approved New Drug Applications for Orally Administered
Levothyroxine Sodium Drug Products; Docket No. 97N-0314

Dear Sir or Madam:

The undersigned respectfully submits this petition on behalf of our client, Jerome Stevens Pharmaceuticals, Inc. (JSP), under the Federal Food, Drug, and Cosmetic Act (FDCA). We request that the Food and Drug Administration (FDA) refuse to extend any further the deadline for manufacturers of orally administered levothyroxine sodium (LS) synthetic thyroid drug products to obtain approved new drug applications (NDAs) as a condition for continuing to market the drug. That deadline has already been extended by one full year to its current date of August 14, 2001.

JSP is a manufacturer of LS. In reliance on the previous FDA regulation requiring NDA submission and approval by August 14, 2000, JSP prepared and submitted a NDA for LS on October 19, 1999 which was approved by FDA on August 21, 2000. JSP has sufficient manufacturing capacity to satisfy demand for the product in the United States if other companies fail to satisfy their regulatory responsibilities.

A. Action Requested

For the reasons stated below, JSP and the undersigned respectfully request that FDA refuse to extend any further the deadline for manufacturers of orally administered LS drug products to obtain approved new drug applications (NDAs) as a condition for continuing to market the drug. That deadline has already been extended by one full year to its current date of August 14, 2001.

B. Statement of Grounds

The current deadline of August 14, 2001 for manufacturers of orally administered LS drug products to obtain approval of their NDAs is itself a significant extension from the initial deadline of August 14, 2000. In light of the concern properly identified by FDA with regard to the potency and stability of orally administered LS drug products, further delay of the deadline would allow potentially unsafe and ineffective products to remain on the market. This situation would create a potential, and unnecessary, risk to public health. With the recent approval of a NDA for JSP's LS product, UNITHROID, there now exists a properly registered and inspected product available to patients in the United States. No medical justification exists to permit unproven products to remain on the

1301 K Street, N.W.
Suite 1100 - East Tower
Washington, D.C. 20005
202.414.9200
Fax 202.414.9299

Delaware
New Jersey
New York
Pennsylvania
Virginia
Washington, DC

market. It would also be unfair to JSP, prescribing physicians and consumers to change the rules to which at least one company was required to faithfully comply.

1. Regulatory Background

Orally administered LS is used as a replacement therapy in conditions characterized by diminished or absent thyroid function, such as cretinism, myxedema, nontoxic goiter, or hypothyroidism.

Levothyroxine sodium was first introduced into the market as a prescription drug before 1962, without an approved NDA, in the belief that it was not a "new drug" as defined by the FDCA. The current regulatory requirements for obtaining new drug approval prior to marketing were implemented in 1962. On August 14, 1997, FDA announced in a *Federal Register* Notice that, as part of its program for Drug Efficacy Study Implementation (DESI), LS must comply with the NDA approval requirements. 62 *Fed. Reg.* 43535 (Aug. 14, 1997).

FDA stated in the Notice that it required manufacturers of LS products to file NDAs due to concerns over potential inconsistencies in the potency and bioavailability of the products' active ingredient. Specifically, FDA noted that thyroid replacement therapy is a lifelong endeavor, requiring individualized, patient-specific dosing. Physicians prescribe a low initial dose, and gradually increase it until clinical evaluation and laboratory testing indicate that an optimal dose has been achieved. Once a patient's dose has been established for an existing product, varying potency or bioavailability of that product, or any other, raises substantial risks. If the drug product is of lesser potency or bioavailability, a suboptimal response and hypothyroidism could result. If the drug product is of greater potency or bioavailability, toxic manifestations of hyperthyroidism could result (e.g., cardiac pain, palpitations, or cardiac arrhythmias).

In light of these expressed concerns, FDA stated that, "it is critical that patients have available to them products that are consistent in potency and bioavailability." The Notice described reported incidents of adverse events due to subpotent or superpotent LS products. It also referenced concerns over changes in product formulations that were not reviewed by FDA, that resulted in unexpected increased potency. Moreover, it noted that LS is unstable in the presence of light, temperature, air, and humidity. FDA cited numerous instances of inadequate stability testing which resulted in uneven product potency and unreliable expiration dates.

FDA concluded properly that none of the orally administered LS products then on the market had been shown to demonstrate consistent potency and stability. They could not be considered generally recognized as safe and effective in the Agency's view. LS was, therefore, deemed a new drug under section 201(p) of the FDCA. Manufacturers were required to submit NDAs, or file citizen petitions evaluating the issue of whether their products were subject to the new drug requirements of the FDCA.

Despite its concern over the potential safety risks presented by LS products, FDA recognized that they were medically necessary to treat hypothyroidism, and that no alternative therapy was available as an adequate substitute in the event that the drug was removed from the market because no company had a FDA approved NDA. Accordingly, it did not implement the new NDA requirement immediately. It gave manufacturers 3 years -- until August 14, 2000 -- to file and obtain approval of NDAs.

On April 26, 2000, FDA published a notice in the *Federal Register* extending the deadline for filing and obtaining approval of NDAs by one additional year to August 14, 2001. 65 *Fed. Reg.* 24488 (April 26, 2000). The basis for the extension was to allow manufacturers additional time to conduct clinical studies and prepare NDA applications. The additional time, in FDA's view, insured that the supply of this medically necessary product would not be disrupted.

2. JSP Has Complied With FDA's Notice and Obtained NDA Approval

In response to FDA's August 14, 1997 *Federal Register* notice, JSP generated and/or gathered the data required to comply with FDA's requirements for the filing of NDAs. On October 19, 1999, JSP submitted an NDA for its product -- NDA 21-210. At the same time, the Company expanded its production capabilities to produce sufficient product to accommodate the total domestic market demand for its product. JSP's NDA was approved on August 22, 2000. FDA approval followed a full pre-approval inspection of JSP's manufacturing facilities to insure compliance with current good manufacturing practices (GMPs).

3. Further Extension of the Deadline is Unnecessary in Light of the Availability of NDA-Approved Product

In light of the availability of orally administered LS with an approved NDA and approved GMP-compliant manufacturing facilities, the basis for extending the deadline again for manufacturers to file and obtain NDA approval no longer applies. There is now available to consumers a LS product proven safe and effective, with consistent potency and bioavailability -- JSP's UNITHROID. Indeed, UNITHROID is the only FDA-approved LS product currently on the American market. The concern that thyroid patients would lose a medically necessary treatment if FDA enforced the NDA requirement no longer applies. FDA's recent extension of the deadline for manufacturers to obtain approved NDAs for orally administered LS, despite providing three year for manufacturers to comply, resulted in an anomaly in the marketplace. A drug product with NDA approval must now compete with products that have not undergone the same required regulatory review. FDA should not expand this inequity and risk to public health by extending a delay in NDA approval now that a compliant product is on the market.

On August 14, 2001, no patient will have to go without an orally administered LS product as the result of other manufacturers' inability to meet the four-year deadline for regulatory approval. Even in the unlikely event that all of the other LS manufacturers were forced to withdraw their products from the market at that time, JSP's UNITHROID would be available to patients with hypothyroidism. As noted above, JSP has increased its production capacity since filing the NDA, and would be able to meet the market demand should the need arise.

In the interest of public health, JSP has undertaken the effort and expense of complying with FDA's notice by the initial deadline. A number of other manufacturers have not yet done so, but may continue to market their products, despite the potential health risks that FDA has identified. To extend the deadline once again when an NDA-approved product is now available, after four years granted by FDA to other manufacturers to come into regulatory compliance, would only perpetuate the risks to public health that FDA has identified and be grossly unfair to compliant manufacturers like JSP. With an NDA-approved product now available, there is no longer any public health rationale for doing so.

Finally, FDA is under firm authority to determine that for reasons connected with the potency and variability from lot-to-lot, the LS is not generally recognized as safe (GRAS) within the meaning of §201(p) of the FDCA. The Agency employed proper procedure pursuant to promulgated regulations under 21 CFR §314.200(e) to consider claims that particular manufacturers make LS that is GRAS. These claims require clinical data similar to the data required to compile an NDA in this circumstance. While citizens petitions have reportedly been filed on behalf of at least one manufacturer contending that LS is GRAS, FDA is within its express statutory and regulatory authority to grant or deny such petitions. Certainly FDA's review of the petition(s) and decision can be made quickly so that the petitioner(s) can determine, in the event of a denial, whether to submit an NDA, or withdraw the product from the market. No delay in the August 14, 2001 date should be necessary as a result of the filing of these petitions.

C. Environmental Impact

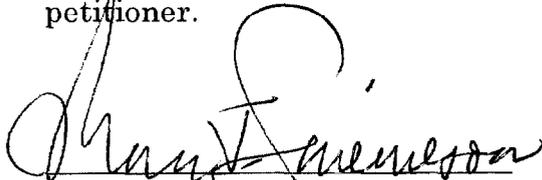
The undersigned claims a categorical exclusion from preparation of an environmental assessment or environmental impact statement under 21 C.F.R. § 25.30.

D. Economic Impact

No information on economic impact has been requested at this time.

E. Certification

The undersigned certifies, that, to his best knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petitioner.

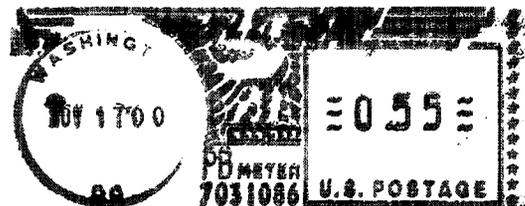


Marc J. Schemeson, Esq.
Regulatory Counsel to Jerome Stevens Pharmaceuticals, Inc.
Reed Smith, LLP
1301 K Street, NW
Washington, DC 20005

cc: Ms. Christine F. Rogers
Mr. Ronald J. Steinlauf

ReedSmithLLP

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