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BY HAND DELIVERY

Dockets Management Branch
Food and Drug Administration
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**COMMENT OF KING PHARMACEUTICALS, INC.
ON PETITION FOR STAY OF ACTION
FILED BY JEROME STEVENS PHARMACEUTICALS, INC.
Docket No. 02P0135**

King Pharmaceuticals, Inc. ("King"), pursuant to 21 C.F.R. §§ 30(d) and 35(h)(3), hereby submits this Comment on the Petition for Stay of Action (the "Petition") filed by Jerome Stevens Pharmaceuticals, Inc. ("Jerome"), Docket No. 02P1035.

While Jerome does not specifically request that the FDA stay any action with respect to King's orally-administered levothyroxine sodium ("LS") drug Levoxyl®, in light of the extraordinary and extensive relief Jerome seeks with respect to LS drugs, King requests that the FDA carefully consider this Comment and the facts set forth herein and deny Jerome's Petition with respect to Levoxyl®.

Introduction

Jerome Seeks Overbroad Relief

In its Petition, Jerome seeks redress from the FDA for disclosure on the FDA website of alleged trade secrets relating to the manufacturing process for Jerome's LS drug Unithroid. Without making any specific allegations of use of its alleged trade secrets by King or any other LS drug makers, Jerome requests that the FDA:

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. . . immediately and indefinitely stay (1) all grants of drug pre-market authority that used, relied on, or were based on Jerome's confidential and trade secret manufacturing information for orally-administered

levothyroxine sodium (LS) and (2) all pending and prospective NDAs and ANDAs that use, rely on, or are based on Jerome's confidential and trade secret manufacturing information for orally-administered LS.

Levoxyl® NDA Did Not Use Jerome's Alleged Trade Secrets

King 1/ submits this comment to clarify that the disclosure of Jerome's alleged trade secrets has nothing to do with the approved Levoxyl® NDA. As set forth below and in the attached Declaration of Thomas Rogers ("Rogers Declaration"), Exhibit 1 hereto:

- the Levoxyl® NDA, which details the formula and manufacturing process for Levoxyl®, was submitted on July 28, 2000, before the claimed disclosure of Jerome's secret manufacturing information on the FDA website on August 22, 2000; and
- none of the amendments to the Levoxyl® NDA after August 22, 2000 altered its formula or manufacturing process. See Rogers Declaration ¶ 17.

Thus, there is no way that the formula or manufacturing process set forth in the Levoxyl® NDA were based on Jerome's alleged trade secrets purportedly disclosed on the FDA website weeks after the Levoxyl® NDA was filed.

Indeed, Jerome makes no direct assertion that its alleged trade secrets are implicated in the Levoxyl® NDA. Furthermore, Jerome itself claims that "Unithroid and Levoxyl would have shared 90% of the orally-administered LS market" had the FDA not disclosed Jerome's alleged trade secrets. 2/ Jerome thus concedes Levoxyl®'s lawful place in the market. Accordingly, King seeks to clarify that Jerome's Petition is not directed at Levoxyl®.

1/ Jones Pharma Incorporated ("Jones"), which filed the Levoxyl® NDA, is now a wholly-owned subsidiary of King, and references to King herein include Jones.

2/ The alleged injury Jerome asserts in its Notice of Claims Pursuant to Federal Tort Claims Act ("Notice"), Exhibit 1 to its Petition, is "based on the assumption that Unithroid and Levoxyl would have shared 90% of the orally-administered LS market" had the FDA not disclosed Jerome's alleged trade secrets. See Notice at 33.

No Legal Basis for Action Against Levoxyl® NDA.

Moreover, there is no legal basis for the FDA even to consider withdrawal of its approval of the Levoxyl® NDA as a remedy for the disclosure of Jerome's alleged trade secrets on the FDA website. Under the Federal Food, Drug and Cosmetic Act ("FFDCA"), approval of an NDA may only be withdrawn after notice and opportunity for hearing to the applicant, and only then for certain specific reasons set forth in the statute. *See* 21 U.S.C. § 355(e). Providing a remedy for the FDA's purported disclosure of another company's alleged trade secrets is not one of the prescribed bases for withdrawal of approval of an NDA under the FFDCA.

In addition, any action against Levoxyl® would wrongly deprive the public of an important drug for the safe and effective treatment of thyroid disease – a drug for which Unithroid is not a therapeutically equivalent substitute. Thus, for these reasons and as more fully set forth below and in the exhibits hereto, King seeks to ensure that no action with respect to the Levoxyl® NDA is considered in response to the Petition.

I. Jerome's Alleged Trade Secrets Not Used in Levoxyl® NDA.

The Levoxyl® NDA was filed July 28, 2000. *See* Notice at 12. The disclosure of Jerome's alleged trade secrets did not occur until August 22, 2000. *See* Petition at 3. The amendments to the Levoxyl® NDA filed after August 22, 2000 do not alter its formula or manufacturing process. As set forth in the Rogers Declaration and evidenced in the amendment cover letters attached thereto, ^{3/} each of the post-August 22, 2000 amendments merely provided additional information requested by the FDA during its review of the Levoxyl® NDA, including additional stability data, dissolution test data, a debarment statement, a request for categorical exclusion for an environmental impact assessment and labeling. None of these amendments incorporated any alleged Jerome trade secrets. Given these circumstances, it is simply not possible that the Levoxyl® NDA used, relied on, or was based on the August 22, 2000 disclosure of Jerome's alleged trade secret manufacturing process on the FDA website.

^{3/} King has made minor redactions to certain of the amendment cover letters to preserve its own confidential, proprietary information.

Because the publicly available version of the Petition does not reveal the nature of Jerome's alleged trade secret manufacturing process, 4/ it is obviously difficult for King to evaluate whether Jerome has valid trade secrets and whether such trade secrets were improperly disclosed by the FDA. For the same reason, it is also difficult for King to state categorically that its own proprietary manufacturing process for Levoxyl® is completely different from the process that Jerome claims as its own. That said, Levoxyl® is not made with same inactive ingredients as Unithroid, 5/ and the Levoxyl® manufacturing process was developed long before any disclosure of Jerome's alleged trade secrets. Furthermore, upon the approval of the Unithroid NDA, King provided the FDA with a certification that the Levoxyl® NDA did not infringe on any known patents. *See* March 19, 2001 Letter from Nancy Cafmeyer to Dr. John Jenkins, Exhibit F to the Rogers Declaration.

It is important to note that Jerome does not assert that its trade secrets are used in making Levoxyl®. Indeed, the money damages Jerome seeks in its Notice are based on the assumption that Unithroid and Levoxyl® would have split 90% of the LS drug market absent the FDA's disclosure of Jerome's alleged trade secrets. *See* Notice at 33. Therefore, given the date of the filing of the Levoxyl® NDA and absent any specific allegations of trade secret misappropriation with respect to the Levoxyl® NDA, the FDA must conclude that the Petition does not seek relief with respect to Levoxyl®. Furthermore, as explained below, there is no legal basis for such relief in any event.

II. No Statutory Basis for Suspension or Withdrawal of FDA Approval of The Levoxyl® NDA.

Jerome Seeks Administrative Stay Without Statutory Basis

Part of the relief requested by Jerome is an immediate and indefinite "stay" of all grants of pre-market authority based on NDAs or ANDAs that "used, relied on, or were based on Jerome's confidential and trade secret manufacturing information." While described by Jerome as a "stay," the relief Jerome seeks with

4/ Jerome's request that the FDA consider certain attachments and information submitted with its Petition but withheld from the public appears to violate 21 C.F.R. § 10.20(j), which requires that all supporting material be on public display and available for public inspection.

5/ For example, Unithroid has starch and acacia as inactive ingredients. *See* Notice at 7 n.13. Levoxyl® does not. *See* Rogers Declaration. ¶ 19.

respect to NDAs that the FDA has already approved amounts to the suspension or withdrawal of NDA approval. Under the FFDCA, the Secretary of Health and Human Services has non-delegable authority to suspend approval of an NDA, but only in the rare event that the Secretary finds "an imminent hazard to the public health," and the applicant must be provided notice of the suspension and opportunity for an expedited hearing. *See* 21 U.S.C. 355(e). The Petition does not assert any potential hazard to public health – the only threat asserted is to Jerome's speculative revenues from Unithroid.

Under the FFDCA, NDA approval may only be withdrawn after notice and opportunity for the applicant to be heard, and only then based on certain specific findings, including new concerns about the safety and effectiveness of the drug, the failure of the applicant to file certain patent information, or the fact that the NDA contains an untrue statement of material fact. *Id.* None of these statutory grounds for withdrawal of NDA approval is asserted in the Petition. ^{6/} With respect to the approved Levoxyl® NDA, the Petition must be denied because Jerome cannot use regulatory administrative stay procedures to obtain relief that is not authorized by the FFDCA.

Jerome Improperly Seeks to Obtain Private Remedy from NDA Process

Jerome's Petition improperly seeks to use the NDA process to provide a private remedy for the purported tortious conduct of the FDA in disclosing Jerome's alleged trade secrets. However, the FFDCA already prohibits the FDA's wrongful

^{6/} In its Notice, Jerome asserts that reserve samples of Levoxyl® used in bioavailability testing were not properly preserved as required by 21 C.F.R. § 320.38. *See* Notice at 30-31. As clarified in King's March 8, 2001 letter to the FDA, although not held by the contract research organization, retention samples for the studies conducted in support of the Levoxyl® NDA have been maintained by the NDA sponsor. *See* March 8, 2001 Letter from Nancy Cafmeyer to Dr. John Jenkins, Rogers Declaration Exhibit D. Thus, contrary to Jerome's implication, samples are appropriately available for verification of Levoxyl® bioavailability testing data. Likewise, Jerome's speculation in the Notice regarding the potential effect of software errors on Levoxyl® testing data (Notice at 31-32) is baseless, given that the minor software malfunction noted by the FDA was fully addressed and the testing data re-validated to the FDA's satisfaction, as evidenced by its approval of the Levoxyl® NDA. *See, e.g.,* March 26, 2001 Letter from Herbert W. Smith to Charles W. Sedgewick, Rogers Declaration Exhibit N; FDA letter approving Levoxyl® NDA, Rogers Declaration Exhibit M.

disclosure of trade secrets under criminal penalty, *see* 21 U.S.C. § 331(j), and Jerome is already seeking monetary compensation for its alleged injury under the Federal Tort Claims Act ("FTCA"). Given (a) that the Petition does not assert any statutory basis for suspension or withdrawal of an approved NDA, and (b) the existence of other available legal remedies for the FDA's alleged misconduct, no "stay" of any approved NDA is appropriate.

Jerome's Petition is Untimely with Respect to Levoxyl®

Furthermore, specifically with respect to the Levoxyl® NDA approved on May 25, 2001, a timely petition to stay its effect under 21 C.F.R. § 10.35 would have to have been filed within 30 days of the decision, i.e., no later than June 24, 2001. *See* 21 C.F.R. § 10.35(g) ("A petition for stay of action submitted later than 30 days after the date of the decision involved will be dismissed as untimely unless the Commissioner permits the petition to be filed after 30 days."). At the time the Levoxyl® NDA was approved in May 2001, Jerome had known about the disclosure of its alleged trade secrets on the FDA website for several months. If, as a result of the disclosure, Jerome believed that a stay of approval of the Levoxyl® NDA was warranted because of potential irreparable harm, Jerome was obliged to seek such stay within the afforded 30-day period. Jerome, however, did not file its Petition until March 26, 2002, more than ten months after approval of the Levoxyl® NDA. Thus, with respect to Levoxyl®, the Petition is untimely and no relief is procedurally available.

III. No Public Policy or Public Interest Justifies Withdrawal of Approval of The Levoxyl® NDA.

Most importantly, there is no public policy or public health justification for any action with respect to the Levoxyl® NDA. Levoxyl® is a valuable drug deemed by the FDA to be safe and effective for the treatment of thyroid disease. More than 20 million Levoxyl® prescriptions were written in the United States from May 5, 2001 through May 3, 2002 (compared with less than one million prescriptions for Unithroid in the same time period). *See* Rogers Declaration ¶ 20. It is clearly in the public interest to ensure continued availability of Levoxyl®, thereby promoting public health and choice for consumers. This is particularly true given the lack of any suggestion that Jerome's alleged trade secrets are used in the manufacture of Levoxyl®.

Furthermore, as the FDA recognized when it required NDAs to be submitted for LS drugs, LS has a narrow therapeutic-toxicity range and health hazards can arise from even minor changes in potency. 7/ These health risks increase when patients are moved from one LS drug to another. 8/ The FDA has assigned BX therapeutic equivalence codes to Unithroid and Levoxyl®, so the two drugs are deemed to be therapeutically inequivalent. 9/ According to the FDA's own Guidance statement, "several physician office visits over as much as 6 months to one year may be necessary to adjust optimally the dose of a new [LS] product." 10/

If Levoxyl® were no longer available, thyroid patients forced to switch to Unithroid or another LS drug would be subject not only to (a) additional physician visits, tests and costs associated with dosage retitration and monitoring, but also (b) the risk of adverse health effects associated with undertreatment or overtreatment until the dosage of the new product was optimally adjusted. Thus, the detriment to public health associated with the withdrawal of approval of the Levoxyl® NDA would far outweigh any private remedial interest arising out of the FDA's disclosure of Jerome's alleged trade secrets.

Certification

The undersigned certify that, to the best of their knowledge and belief, this comment contains all information and views on which the comment relies, and that it includes representative data and information known to the undersigned which are unfavorable to the comment.

7/ See 62 FR 43535 at 43536 (Aug. 14, 1997), Exhibit 2 hereto; see also Notice at 4-5 n.8.

8/ *Id.*

9/ See *FDA Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"); see also FDA Center for Drug Evaluation and Research, *Guidance for Industry: Levothyroxine Sodium Products, Enforcement of August 14, 2001 Compliance Date and Submission of New Applications (July 2001)* (the "July 2001 Guidance") at 5, Exhibit 3 hereto.

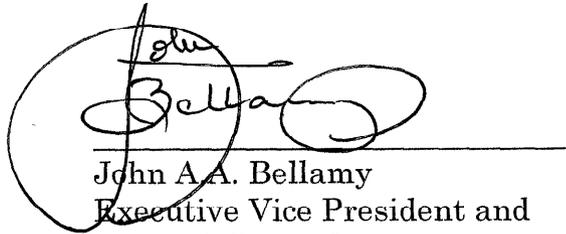
10/ July 2001 Guidance at 2 n.3.

Conclusion

As clarified above, Jerome's claims regarding FDA disclosure of its alleged trade secrets have nothing to do with FDA approval of the Levoxyl® NDA. Jerome has not requested suspension or withdrawal of approval of the Levoxyl® NDA, nor is there any legal basis for the FDA to do so. For these reasons, King respectfully requests that Jerome's Petition be denied with respect to Levoxyl®.



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