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December 30, 2005

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

Re: Citizen Petition re Date of Approval for Lunesta™ (Eszopiclone) Tablets

Dear Sir or Madam:

Sepracor Inc. (Sepracor) submits this petition pursuant to 21 C.F.R. 10.35.

A. ACTION REQUESTED

Sepracor requests that the Commissioner of Food and Drugs take the following actions:

1. Confirm that the approval of the NDA for Lunesta™ (eszopiclone) tablets (Lunesta) became effective on April 4, 2005.

2. Confirm that the five-year exclusivity for Lunesta commenced on the date of effective approval, April 4, 2005.

3. Confirm that the patent-term extension for Lunesta should be calculated based on the date of effective approval, April 4, 2005.

B. STATEMENT OF GROUNDS

Background

FDA issued an approval letter for Sepracor's NDA for Lunesta on December 15, 2004. The active ingredient in Lunesta, eszopiclone, is a new molecular entity,. Sepracor is therefore entitled to a five-year period of exclusivity under Sections 505(c)(3)(D)(ii) and 505(j)(5)(F)(ii) of the Food, Drug, and Cosmetic Act (FDCA) commencing on the date of Lunesta's approval under section 505 of the FDCA. Under 35 U.S.C. 156, Sepracor is also entitled to a patent term extension, which must be calculated based on the date of approval of Lunesta under section 505.

As a matter of law, the date of approval of a drug under section 505 is the date that the agency grants final effective approval to market the drug under the labeling approved by the agency under section 505. In the case of Lunesta, this final effective approval did not occur on December 15, 2004, when the agency issued an "approval" letter to Sepracor. Rather, it occurred several months later, after the Drug Enforcement Administration (DEA) completed the rulemaking process by which Lunesta was

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classified as a Schedule IV controlled substance under the Controlled Substances Act (CSA)

Sepracor's initial proposed labeling for Lunesta, submitted to FDA as part of Sepracor's initial NDA submission on January 30, 2003, did not propose or presume that Lunesta would be considered a controlled substance. Prior to the issuance of its December 2004 approval letter, however, FDA required Sepracor to amend its proposed labeling for Lunesta to include the following statement:

> **Controlled Substance Class**
> [Lunesta] is classified as a Schedule IV controlled substance by federal regulation.

(Emphasis in original.)

This requirement was communicated in an Approvable Letter issued on February 4, 2004, which stated that the agency had "determined that [Lunesta] should be placed in Category IV of the Controlled Substances Act."[1] It was Sepracor's understanding that FDA would be recommending to DEA that eszopiclone be classified as a schedule IV controlled substance under the CSA. In the agency's subsequent approval letter of December 15, 2004, the agency attached draft labeling that was further amended to bear a "C-IV" designation. The statement and designation regarding schedule IV classification were thus conditions of approval for Lunesta.

On December 23, 2005, Sepracor commenced importation of Lunesta into the United States for marketing. The importer notified DEA of the importation and, to Sepracor's surprise, DEA personnel indicated that they had not received a scheduling recommendation from the Department of Health and Human Services (HHS). (The HHS recommendation, which is based on a scheduling recommendation from FDA, is hereinafter referred to as the "HHS/FDA" recommendation.) Although DEA personnel initially suggested to Sepracor that DEA might have jurisdiction over the product, DEA ultimately acknowledged that it had no such jurisdiction because the product had not been classified as a controlled substance.[2]

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[1] Letter to Sepracor, Inc., from Robert Temple, FDA, re NDA 21-476 (Feb. 4, 2004) at 3. The wording was provided in the form of a revised draft of labeling originally submitted by Sepracor.

[2] A "controlled substance" is "a drug or other substance, or immediate precursor, included in schedule I, II, III, IV, or V of [the Controlled Substances Act ("CSA")]. At the time of its importation Lunesta was not included in any of those schedules.

Because Lunesta was not a controlled substance, DEA required that Sepracor obtain special permission to store Lunesta as a non-controlled substance in a controlled substance secured area. Sepracor submitted this request on January 12, 2005. Letter to Christine A. Sannerud, Ph.D., DEA, from Davie G. Adams, Counsel to Sepracor (January 12, 2005) (Tab A).

DEA did not receive the HHS/FDA recommendation for scheduling until January 18, 2005.[3] While this permitted DEA to commence the scheduling process, DEA personnel estimated that scheduling of Lunesta might take three to five months.[4]

On January 18, Sepracor submitted a letter to FDA proposing a plan for marketing Lunesta under special voluntary controls pending completion of the scheduling process.[5] In response to this letter, FDA personnel conveyed to Sepracor informally that the agency expected Sepracor to refrain from marketing Lunesta prior to DEA scheduling and that the agency was prepared to take action against Sepracor if the company did not comply. FDA personnel noted in this regard that (1) Lunesta's labeling displayed the C-IV designation and stated that the product was classified as schedule IV controlled substance when such was not the case and (2) Sepracor had signed an agency form for submission of an NDA that contained the following stipulation:

> If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision."[6]

FDA personnel nevertheless agreed to entertain a more detailed proposal from Sepracor to market Lunesta prior to scheduling under certain strict controls. Sepracor followed up with submissions to the agency on January 25[7] and on January 28.[8] On February 11, 2005, FDA informed Sepracor informally that the agency would not agree to Sepracor's proposal and that Sepracor should not market Lunesta until completion of the DEA scheduling process.

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[3] 70 Fed. Reg. 16935 (2005). Sepracor had numerous contacts with FDA personnel in an effort to facilitate the recommendation regarding scheduling. FDA personnel generally indicated that they were uncertain as to what had happened with regard to the agency's intended recommendation..

[4] *Id.*

[5] The company proposed the following:

> We believe that any potential issues arising out of marketing prior to scheduling can be addressed and the product can be launched responsibly prior to completion of scheduling. If the product is launched at this time and DEA scheduling is not expected for three to five months, DEA registrants should be advised that the product is recommended for scheduling but is not yet scheduled. These registrants (including wholesalers, pharmacies and those physicians who may handle samples of the product) might be informed of these facts through a direct communication from Sepracor. Sepracor might advise these registrants to handle and distribute Lunesta in the same manner that they would handle and distribute a schedule IV controlled substance. Sepracor might provide information on DEA requirements related to records, reports, and storage in the secured area for controlled substances based on advice from DEA. Sepracor would provide registrants with support and follow-up on these issues in coordination with DEA.

Id. at 2.

[6] Form FDA 356h at 2.

[7] Letter to Douglas Throckmorton, M.D., CDER, from Stewart Mueller, Sepracor, re NDA 21-476 (January 25, 2005).

[8] Letter to Douglas Throckmorton, M.D., CDER, from Stewart Mueller, Sepracor, re NDA 21-476 (January 28, 2005).

On April 4, DEA completed the scheduling process for Lunesta. Sepracor then launched Lunesta, 110 days after FDA issuance of the Lunesta approval letter.

Discussion

1. FDA Did Not Grant a Final Effective Approval on December 15, 2004.

(a) The Approval Was Conditioned on Labeling that the Agency Deemed Misleading when the Approval Letter Was Issued.

The December 15, 2004 approval letter for Lunesta contained an important condition: the labeling for Lunesta must be identical to the labeling enclosed with the approval letter, which included a C-IV designation and a statement that the product was classified as a schedule IV controlled substance. Under FDA's interpretation of the FDCA, the marketing of Lunesta without the approved labeling bearing this information would have been considered a violation of FDCA § 301(d) (introduction into interstate commerce of an unapproved new drug).

On the other hand, the marketing of Lunesta *with* the approved labeling would have been considered a violation of FDCA § 502(a) (labeling that is false or misleading in any particular). Agency personnel communicated to Sepracor informally that the marketing of Lunesta with the labeling bearing the C-IV designation and statement that Lunesta is classified as a controlled substance would render the product misbranded under section 502(a) because the product had not yet been classified as a controlled substance. FDA personnel not only suggested that the marketing of Lunesta with the C-IV designation would be illegal, but also threatened severe consequences should Sepracor market the product prior to DEA approval.[9]

Thus the approval letter for Lunesta required Sepracor to submit final printed labeling with a C-IV designation and statement regarding classification as a controlled substance even though, on the date the letter was issued, the agency considered such labeling to misbrand the product and preclude marketing. Because this letter did not authorize marketing of the product with the approved labeling on the date of its issuance, it did not convey final effective approval on that date. Although the letter *purported* to convey an effective approval on the date of issuance, it actually conveyed a contingent approval that would become effective if and when DEA classified Lunesta as a schedule IV controlled substance.

(b) FDA Had No Authority to Grant Final Effective Approval Based on Labeling that the Agency Deemed Misleading.

The approval letter's reference to approval "effective on the date of this letter" must give way to the law and the facts. Section 505(d) of the FDCA provides the criteria

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[9] January 21, 2005, teleconference between Sepracor and FDA.

for approval of an NDA.[10] Section 505(d)(7) precludes the approval of an NDA if the agency deems the product's labeling to be "false or misleading in any particular." This is the same requirement, in precisely the same wording, that is set forth in FDCA § 502(a). Thus under section 505(d)(7) the agency is expressly denied authority to approve a product that is misbranded under section 502(a).

Because the agency conditioned the approval of Lunesta on labeling stating that the product had been classified as a controlled substance, the bar of section 505(d) against approval based on false or misleading labeling could be removed only when the product was classified as stated in the labeling. Although, FDA could have issued a final approval without requiring a specific statement in labeling with regard to classification under the CSA,[11] the agency had no authority to convey final effective approval of Lunesta with the labeling attached to the approval letter until the product was classified as a controlled substance. The agency's December 15, 2004, approval letter must accordingly be deemed a contingent action that became final and effective when (1) the implicit condition of approval – classification as a controlled substance – was satisfied and (2) the explicit condition of approval – labeling stating that the product had been so classified – was rendered nonmisleading and lawful under the FDCA.

(c) A Final Effective Approval Must Be Based on Labeling that Permits Lawful Marketing under the FDCA.

It is clear under case law that the date of approval under section 505 must be determined based on the date on which the agency conferred an immediate right to market under the labeling approved under section 505. In *Norwich Eaton Pharmaceuticals, Inc., v. Bowen*,[12] the United States Court of Appeals for the Sixth Circuit reviewed a lower court's ruling that an FDA approval letter did not constitute a final effective approval under section 505. Although the Sixth Circuit reversed the lower court's decision, the circuit court's reasoning demonstrates why the December 15, 2004, action on Lunesta did not constitute a final effective approval.

The case involved FDA's approval of Buprenex™ (buprenorphine hydrochloride) Injectable (Buprenex), which at the time of the agency's action was classified as a schedule II controlled substance but was proposed for reclassification into schedule V (which would have provided *fewer* controls under the CSA). FDA issued an approval letter for Buprenex based on draft labeling that *did not specify the DEA classification of the product*. Norwich Eaton petitioned FDA to deem the approval letter a conditional approval because, according to the company, "there was no approved label under which the drug could have been marketed; thus, there was no valid approval."[13]

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10 FDCA § 505(c) requires approval of an NDA submitted under section 505(b) unless the agency finds grounds for denial of approval under section 505(d).

11 *See, e.g., Norwich Eaton Pharmaceuticals, Inc., v. Bowen*, 808 F.2d 486, 488 (6th Cir. 1987).

12 808 F.2d 486 (6th Cir. 1987) (*rev'g* 645 F. Supp. 321 (S.D. Ohio 1986).

13 *Id.* at 488.

The Sixth Circuit accepted the proposition that a final effective approval must confer the immediate right to market the product under the approved labeling, but disagreed with the district court's finding that Norwich Eaton could not have marketed Buprenex immediately based on the approved labeling. The circuit court noted that the approval letter did not require the product labeling to state incorrectly that the product had been classified as a schedule IV controlled substance, and concluded as follows:

> Thus Norwich could have marketed the drug at the time of the 1981 approval as a Schedule II drug. It decision not to do so was a marketing decision, *not a result compelled by law.*[14]

In the case of Lunesta, the agency's approval letter required that the product's labeling state incorrectly that Lunesta had been classified as a schedule IV controlled substance. Sepracor's delay of the launch of Lunesta until completion of DEA classification was not a marketing decision. Indeed, it was not a decision at all; but was rather a result compelled by FDA's interpretation of the law.

(d) FDA Intended that the Lunesta Approval Become a Final Effective Approval on the Date of DEA Scheduling.

Despite the wording of the Lunesta approval letter, the agency never regarded the letter as conveying an immediately effective approval to market Lunesta under the FDCA. The agency made clear to Sepracor that, until completion of DEA scheduling, FDA regarded the marketing of Lunesta as unlawful and subject to regulatory action.

The agency also referred repeatedly in its discussions with Sepracor to Form FDA 356h, a transmittal form required to accompany any NDA or any supplement to an NDA. This form required Sepracor to certify that, should FDA propose the product for DEA scheduling, the company would not market the product until scheduling was completed. Had Sepracor not signed the certification, FDA would have refused to file the NDA.[15] Following the issuance of the approval letter, FDA made clear to Sepracor that the agency considered the company bound by the certification and subject to a harsh response if the company failed to comply with it.

FDA cannot, of course, condition the submission of an NDA meeting the requirements of section 505(b) on an additional requirement that an applicant waive its right to market its product upon approval. Such a requirement would be unlawful and unconscionable.[16] The certification requirement must thus be understood to imply that an

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[14] *Id* at 492 (emphasis added).

[15] 21 C.F.R. 314.101(d)(1).

[16] The FDCA provides a statutory right to submit an NDA to the agency and provides a statutory right to an approval in the absence of a finding of a specifically enumerated basis for denying approval. The statute provides that any person may submit an NDA if the NDA meets the clear and express requirements of section 505(b). This is an important right because the agency is required under section

approval action prior to DEA scheduling is deemed contingent and that final effective approval will occur only upon completion of scheduling.

FDA clearly did not intend its December 2004 approval letter to convey an immediate right to market Lunesta under the FDCA. It rather intended that the letter convey a conditional right to market Lunesta under the FDCA – and that a final effective right to market Lunesta under the labeling approved under section 505 be conveyed only upon DEA classification of the product as a schedule IV controlled substance.

2. Lunesta's Five-Year Exclusivity Commenced on April 4, 2005.

Because eszopiclone was a new chemical entity when approved in the Lunesta NDA, Sepracor is entitled to exclusivity under FDCA §§ 505(c)(3)(D)(ii) and 505(j)(5)(D)(ii). This exclusivity precludes the submission of certain ANDAs and 505(b)(2) NDAs for products containing eszopiclone for five years "from the date of the approval" of the Lunesta NDA under section 505. Because the final effective approval of Lunesta occurred on April 4, 2005, when the DEA-scheduling condition of approval was satisfied, the "date of the approval" upon which the five-year exclusivity commenced was April 4, 2005.

3. Lunesta's Review Period for Purposes of Patent Term Extension Ended on April 4, 2005.

The approval of the Lunesta NDA entitled Sepracor to a patent term extension under 35 U.S.C. § 156. Sepracor has submitted to the United States Patent Office a request for extension of United States Patent No. 6,444,673 in accordance with 35 U.S.C. § 156(d).[17] The patent extension is based on a determination of the regulatory review

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505(c) to approve an NDA meeting the terms of section 505(b) unless the agency makes an enumerated finding under section 505(d) that would require denial of approval.

FDA cannot deny an applicant the right to submit an NDA based on criteria outside of section 505(b). The requirement that an applicant certify that it will not market a product until DEA scheduling is complete, even if FDA grants the product an "approval" under the FDCA, is clearly beyond the scope of section 505(b) and clearly beyond the authority of the agency.

[17] Although Sepracor submitted this request based on FDA's stated "approval" date of December 15, 2004, Sepracor did so only to ensure that its right to patent extension be deemed timely and not waived. Sepracor stated in its request as follows:

> On December 15, 2004, the FDA issued an "approval letter" for Sepracor's LUNESTA™ (eszopiclone) NDA under Section 505 of the FDC Act. Although FDA takes the position that the product was "approved" on that date for purposes of determining patent term extension, Sepracor questions whether "the product received permission for commercial marketing" on that date within the meaning of the statute. Sepracor notes that FDA has taken the position that Sepracor cannot market LUNESTA™ under the terms of the "approval letter" until the product is listed on the Schedule of Controlled Substances under 21 USC §823. Nonetheless, in order to avoid potential forfeiture under 35 USC §156(d)(1) based on FDA's current interpretation of the statute, Sepracor submits this request for extension based on FDA's determination that LUNESTA™ was "approved" for purposes of patent term extension on December 15, 2004. In so doing, Sepracor does not waive its right to challenge that determination by FDA.

period for the Lunesta NDA, which is based in part on the time between the date the NDA was submitted under section 505(b) and the date the "application was approved under [section 505]."[18]

FDA must determine this regulatory review period under 21 C.F.R. 60.20-22. For purposes of determining the regulatory review period for Lunesta under these regulations, the date of the final effective approval under section 505 was April 4, 2005.

4. Sound Policy Reasons Support this Outcome

The difficulties and uncertainties resulting from the conditional approval of Lunesta in December 2004 flowed from the desire on the part of FDA and DEA that drugs recommended by FDA for scheduling under the CSA not be marketed until scheduling controls are in place. The problem faced by the two agencies is that Congress did not provide such authority to either agency. Moreover, Congress addressed the issue expressly in the CSA by providing DEA authority to temporarily schedule a drug. This authority is limited by Congress to drugs that DEA determines should be classified as schedule I (maximum controls) "to avoid an imminent hazard to the public safety."[19] It is also limited to drugs for which no "approval is in effect" under section 505.[20] It is thus clear that Congress intended that for drugs approved under section 505, and for drugs that are to be classified as schedule IV, the controls of the CSA not be imposed until the completion of the notice-and-comment scheduling process.

FDA and DEA have long sought in other ways to avoid or prevent the marketing of drugs that the agencies believe should be scheduled but that have not yet been scheduled. The agencies have in the past cooperated to begin DEA's scheduling procedures prior to FDA's expected approval action, so that DEA scheduling would occur near in time to the date of the FDA approval.[21] FDA has also, however, attempted to prevent marketing prior to DEA scheduling by conditioning approval on labeling stating the drug is scheduled and by requiring a certification from the NDA applicant that the product will not be marketed prior to scheduling.

Request for Extension of Patent Term Under 35 U.S.C. § 156 (Tab B, exhibits omitted). In *Unimed, Inc., v. Quigg*, 888 F.2d 826, 828 (Fed. Cir. 1989), the Federal Circuit noted in dicta that the date of approval for purposes of calculating the application period should be the same as the date of approval for purposes of calculating the regulatory review period. The *Unimed* court addressed a different factual situation in which the FDA approval was not conditioned upon DEA scheduling but the FDA approval letter noted that the CSA prohibited marketing of the product under the DEA schedule in effect at the time of the FDA approval. *Id.*

18 *See* 35 U.S.C. § 156(g)(1)(B).

19 21 U.S.C. § 811(h)(1).

20 *Id.*

21 In the case of the sleep disorder drugs Sonata® (zaleplon) Capsules and Provigil® (modafinil) Tablets, DEA scheduling was accomplished within 34 days of the issuance of FDA's approval letter.

These restrictions are beyond FDA's authority; and they are especially inappropriate in the case of Lunesta, where neither FDA nor DEA deemed the scheduling of the drug to be worthy of administrative priority. Had FDA and DEA deemed scheduling of Lunesta prior to marketing to be an important outcome, the agencies could have coordinated the approval and scheduling processes to avoid a hiatus between the issuance of an approval letter and completion of scheduling. The timing of DEA scheduling is determined by (1) the date FDA makes a scheduling recommendation and (2) the efficiency of the DEA scheduling process.

The failure of the two agencies to coordinate the approval and scheduling processes is a function of their priorities. It is also a function of FDA's willingness to utilize extra-legal mechanisms to prevent companies from marketing their "approved" drugs prior to DEA scheduling. While FDA appears to believe that scheduling controls are important enough to justify conditioning approval on completion of DEA scheduling, neither FDA nor DEA believe that such controls are important enough to warrant coordination of FDA scheduling recommendations and DEA scheduling procedures.

In the case of Lunesta, the HHS/FDA scheduling recommendation was not provided to DEA until 35 days after FDA issued its approval letter. FDA personnel gave different accounts of the agency's handling of the scheduling recommendation, including admissions that the internal documentation for the recommendation simply could not be found.

DEA could have utilized expedited rulemaking procedures for scheduling Lunesta but refused to do so, even as the agency conceded that the CSA did not prohibit – and that DEA would not seek to prohibit – the marketing of Lunesta as a non-controlled substance. DEA clearly does not regard the marketing of products prior to imposition of schedule IV controls to be a significant public health issue. In the case of dichloralphenazone, for example, which was initially marketed as a non-controlled substance and subjected to scheduling while it was on the market, DEA delayed the effective date of schedule IV controls for additional 30-day and 60-day periods after completion of scheduling.[22]

While FDA personnel indicated to Sepracor that marketing of Lunesta prior to scheduling was inappropriate from a public health perspective and would be dealt with harshly, neither FDA nor DEA were concerned enough over the public health to coordinate and expedite their responsibilities to ensure the scheduling of Lunesta in a timely manner. Instead, FDA issued an approval letter within the agency's user-fee deadline that conditioned approval on completion of DEA scheduling.

Although FDA's authority to condition an approval on the completion of DEA scheduling is questionable, Sepracor does not seek in this petition to challenge that authority. Sepracor seeks only an acknowledgment by FDA that the approval was, in fact and under law, conditioned on the completion of DEA scheduling and was not final and

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22 68 Fed. Reg. 42,943 (2001).

effective until the condition was met. Should the agency fail to acknowledge the contingent nature of its action, it (1) will have deprived Sepracor of the ability to market Lunesta under approved labeling for 110 days after issuance of its approval letter and (2) will compound this injustice by depriving Sepracor of its statutory right to the full term of protection intended and accorded by Congress under the five-year exclusivity provisions and patent term restoration provisions.

Conclusion

In the final analysis, if FDA and DEA believe it important to ensure that a drug is scheduled prior to marketing, the two agencies should be prepared to set priorities necessary to ensure that FDA approval and DEA scheduling are coordinated. If the agencies do not deem scheduling controls important enough to warrant such coordination, FDA cannot responsibly contend that scheduling controls are important enough to warrant contingent approvals that would deny an NDA holder the right to market its product upon the issuance of an approval letter. Where, as here, FDA has nevertheless imposed such conditions on an approval, the agency must acknowledge the conditional nature of the approval to ensure that Sepracor is at least accorded the full measure of statutory protections provided under the exclusivity and patent term restoration provisions of the FDCA. These rights are important to Sepracor and the company is prepared to validate them in court if necessary.

C. ENVIRONMENTAL IMPACT

As provided in 21 C.F.R. § 15.30 neither an environmental assessment nor an environmental impact statement is required.

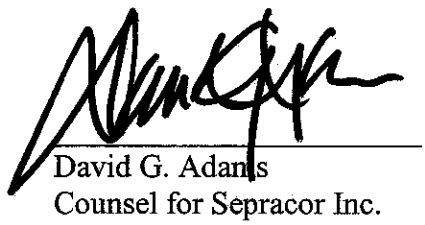
D. ECONOMIC IMPACT

As provided in 21 C.F.R. § 10.30(b) economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

E. CERTIFICATION

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

Respectfully submitted,



David G. Adams
Counsel for Sepracor Inc.

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January 12, 2005

VIA FACSIMILE AND U.S. MAIL

Christine A. Sannerud, Ph.D.
Chief, Drug & Chemical Evaluation Section
Drug Enforcement Administration
600 Army-Navy Dr.
Rm. E6233
Arlington, VA 22202

Re: Request for Exception to Store Non-Controlled Substance in Secured Storage Area

Dear Dr. Sannerud:

Sepracor Inc. (Sepracor) respectfully requests a limited exception from the requirement in 21 C.F.R. 1301.72(b)(8)(ii) that registrants secure written permission the Special Agent in Charge of DEA for their area in order to store a non-controlled substance in their secured area for controlled substances. Sepracor seeks this exception pursuant to 21 C.F.R. 1307.03[1] for its product Lunesta™ (eszopiclone) Tablets (Lunesta), which is not a controlled substance but which the Food and Drug Administration is recommending that DEA schedule as schedule IV.

This exception would ensure that any registrant receiving a stock of Lunesta will be able to provide the same security for Lunesta as would be provided for a controlled substance. Given FDA's conclusion that Lunesta should be scheduled, Sepracor believes that it would be appropriate for distributors of Lunesta to provide this level of security immediately.

Sepracor's distributor, Cord Logistics, has already requested written permission to store Lunesta in a secured controlled substance area, and Sepracor expects that other registrants receiving Lunesta will want to provide the same security. This form of security for Lunesta is appropriate and is consistent with 21 C.F.R. 1301.72(b)(8)(ii).[2] Because these registrants will be

[1] Section 1307.03 provides that "[a]ny person may apply for an exception to the application of any provision of this chapter by filing a written request stating the reasons for such exception."

[2] Section 1301.72(b)(8)(ii) provides as follows:

> (ii) Non-controlled drugs, substances and other materials may be stored with Schedule III through V controlled substances in any of the secure storage areas required by 21 CFR 1301.72(b), provided that permission for such storage of non-controlled items is obtained in advance, in writing, from the Special Agent in Charge of DEA for the area in which such storage area is situated. Any such permission tendered must be

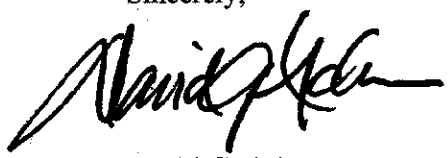
handling Lunesta in the same manner as a controlled substance, the use of the controlled substance area will not diminish security effectiveness of other controlled substances.

Although each registrant handling Lunesta could individually seek written permission from the Special Agent in Charge of their area, we believe it would be more efficient for DEA to grant a general exception from this requirement for Lunesta pursuant to 21 C.F.R. 1307.03, which could be communicated by Sepracor or its distributors to each registrant receiving Lunesta. This would reduce the administrative burden on DEA and would ensure that registrants receiving Lunesta will not have to hold the product in a less secure environment pending written permission from the respective Local Agents in Charge.

We have discussed this proposal in some detail with Charles Trant, Office of the Chief Counsel.

We would appreciate your expeditious handling of this request to ensure that registrants receiving Lunesta will have proper and immediate access to a secured area for storage of a product recommended for scheduling. If you have any questions, please feel free to call me at (202) 344-8014.

Sincerely,



David G. Adams
Counsel for Sepracor

cc: Charles Trant

upon the Special Agent in Charge's written determination that such non-segregated storage does not diminish security effectiveness for Schedules III through V controlled substances.

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BOX PATENT EXT.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No. 0701.243

In re: U.S. Patent No. 6,444,673

Patentee: Claude COTREL, *et al.*

Assignee: Sepracor Inc.

Issue date: September 3, 2002

REQUEST FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. §156

Director of the United States Patent and Trademark Office

Washington, D.C. 20231

BOX PATENT EXT.

Sir:

Pursuant to Section 201(a) of the Drug Price Competition and Patent Term Restoration Act of 1984, 35 U.S.C. § 156, Sepracor Inc. ("Sepracor"), represents that it is the owner of record of United States Patent No. 6,444,673 and hereby requests an extension of the patent term of U.S. Patent No. 6,444,673.

The following information is submitted in accordance with 35 U.S.C. § 156(d) and 37 C.F.R. § 1.740, and follows the format and requirements set forth in 37 C.F.R. § 1.740.

(1) "A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics;" 37 C.F.R. §1.740(a) (1).

The approved[1] product is LUNESTA™ (eszopiclone), film-coated tablets, 1 mg, 2 mg and 3 mg, for oral administration. The generic name for the approved product is eszopiclone, which is indicated for the treatment of insomnia, including difficulty falling asleep and/or maintaining sleep.

Synonyms for eszopiclone are:

ESTORRA™;

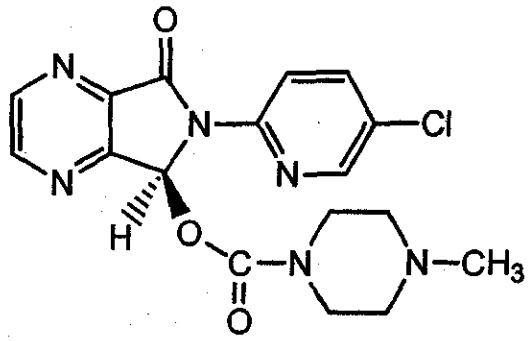
esopiclone;

(+)-zopiclone; and

(S)-zopiclone.

The eszopiclone is identified by the following:

(a) Structural Formula:



(b) Chemical names:

[1] As described more fully on pages 3-4, this request for extension is submitted based on FDA's determination that LUNESTA™ was "approved" on December 15, 2004, for purposes of determining patent term restoration. Sepracor questions this determination by FDA and does not waive its right to challenge that agency determination following submission of this request for extension.

(+)-(5S)- 6-(5-chloro-2-pyridyl)-5-[(4-methyl-1-piperazinyl)carbonyloxy]-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazine;

(+)-(5S)-6-(5-chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazin-5-yl 4-methylpiperazine-1-carboxylate; and

1-Piperazinecarboxylic acid, 4-methyl-, (5S)-6-(5-chloro-2-pyridinyl)-6,7-dihydro-7-oxo-5H-pyrrolo[3,4-b]pyrazin-5-yl ester.

(c) Molecular Weight: 388.81

(d) Empirical Formula: $C_{17}H_{17}ClN_6O_3$

(2) "A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred;" 37 C.F.R. § 1.740(a)(2).

Section 505 of the Federal Food, Drug, and Cosmetic Act (FDC Act), 21 U.S.C. § 355, is the Federal statute under which the Food and. Drug Administration's (FDA's) regulatory review of Sepracor's LUNESTA™ investigational new drug (IND) application and new drug application (NDA) for eszopiclone occurred. Section 505(b) of the FDC Act, 21 U.S.C. § 355(b), authorizes the filing of an NDA for a "new drug". The FDA subsequently approved the LUNESTA™ NDA (021-476) under the authority granted the agency by Section 505(c) of the FDC Act, 21 U.S.C. § 355(c).

(3) "An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred;" 37 C.F.R. § 1.740(a)(3).

On December 15, 2004, the FDA issued an "approval letter" for Sepracor's LUNESTA™ (eszopiclone) NDA under Section 505 of the FDC Act. Although FDA takes the position

that the product was "approved" on that date for purposes of determining patent term extension, Sepracor questions whether "the product received permission for commercial marketing" on that date within the meaning of the statute. Sepracor notes that FDA has taken the position that Sepracor cannot market LUNESTA™ under the terms of the "approval letter" until the product is listed on the Schedule of Controlled Substances under 21 USC §823. Nonetheless, in order to avoid potential forfeiture under 35 USC §156(d)(1) based on FDA's current interpretation of the statute, Sepracor submits this request for extension based on FDA's determination that LUNESTA™ was "approved" for purposes of patent term extension on December 15, 2004. In so doing, Sepracor does not waive its right to challenge that determination by FDA.

(4) "In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum- Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved." 37 C.F.R. § 1.740(a)(4).

The active ingredient in LUNESTA™ (eszopiclone) film-coated tablets is eszopiclone. Eszopiclone has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act or the Virus-Serum-Toxin Act. Eszopiclone is the dextrotatory enantiomer of the racemic mixture zopiclone. Zopiclone has not been previously approved by the FDA.

(5) "A statement that the application is being submitted within the sixty day period permitted for submission pursuant to § 1.720(f) and an identification of the last day on which the application could be submitted;" 37 C.F.R. § 1.740(a)(5)

This application is being submitted within the sixty-day period following FDA approval of the LUNESTA™ (eszopiclone) NDA. FDA approved the LUNESTA™ (eszopiclone) NDA on December 15, 2004. The sixty-day period following approval of the NDA for submission of this patent extension application will expire on February 13, 2005.

(6) "A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration;" 37 C.F.R. § 1.740(a)(6).

U.S. Patent No. 6,444,673

Inventors: Claude COTREL and Gerard ROUSSEL

Issue date: September 3, 2002

Expiration Date: January 16, 2012

(7) "A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings;" 37 C.F.R. § 1.740(a)(7).

A copy of U.S. Patent No. 6,444,673 is attached as Exhibit A.

(8) "A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or re-examination certificate issued in the patent," 37 C.F.R. § 1.740(a)(8).

U.S. Patent No. 6,444,673 issued on September 3, 2002. Maintenance fees are not due until March 3, 2006.

No disclaimer, certificate of correction or re-examination certificate has issued to date in connection with U.S. Patent No. 6,444,673.

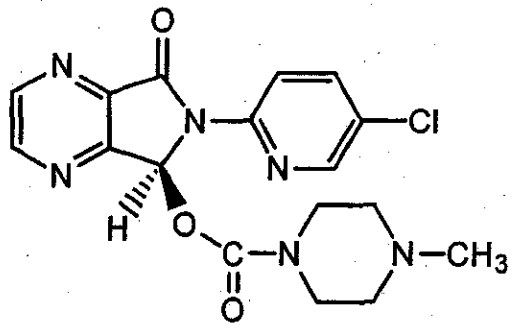
(9) "A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which one such patent claim reads on:

(i) The approved product if the listed claims include any claim to the approved product;

(ii) The method of using the approved product, if the listed claims include any claim to the method of using the approved product;

(iii) The method of manufacturing the approved product, if the listed claims include any claim to the method of manufacturing the approved product;" 37 C.F.R. §1.740(a)(9).

U.S. Patent No. 6,444,673 claims the approved product eszopiclone. Claims 1, 3 and 4 are directed to the dextrorotatory isomer of 6-(5-chloro-2-pyridyl)-5-[(4-methyl-1-piperazinyl)carbonyloxy]-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazine and pharmaceutically acceptable salts thereof. Claims 2, and 5-8 are directed to a pharmaceutical composition comprising eszopiclone. Eszopiclone is the generic name for the dextrorotatory isomer of 6-(5-chloro-2-pyridyl)-5-[(4-methyl-1-piperazinyl)carbonyloxy]-7-oxo-6,7-dihydro--5H-pyrrolo[3,4-b]pyrazine and has the following formula:



Representative claims of U.S. Patent No. 6,444,673 are reproduced below.

1. 6-(5-chloro-2-pyridyl)-5-[(4-methyl-1-piperazinyl)carbonyloxy]-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazine, or a pharmaceutically acceptable salt thereof, in the form of its dextrorotatory isomer and essentially free of its levorotatory isomer.

2. A pharmaceutical composition comprising an effective amount of the dextrorotatory isomer, essentially free of the levorotatory isomer of 6-(5-chloro-2-pyridyl)-5-[(4-methyl-1-piperazinyl)-carbonyloxy]-7-oxo-6,7- dihydro-5H-pyrrolo[3,4-b]pyrazine, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

(10) A statement, beginning on a new page of the relevant dates and information pursuant to 35 U.S.C. § 156(g) in order to enable the Secretary of Health and Human Services, or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

(i) For a patent claiming a human drug, antibiotic or human biological product:

(A) The effective date of the investigational new drug (IND) application and the IND number;

(B) The date on which a new drug application (NDA) ....was initially submitted and the NDA or PLA number :and

(C) The date on which the NDA was approved or the Product License issued; 37 C.F.R. § 1.740(a)(10)(i).

In order to enable the Secretary to determine the applicable regulatory review period, the following information is provided:

(a) Sepracor Inc. filed its Investigational New Drug (IND) application for LUNESTA™ (eszopiclone) on July 22, 1999 (IND 58,647), and it became effective on August 21, 1999;

(b) Sepracor Inc. initially submitted a new drug application (NDA) for LUNESTA™ (eszopiclone) to the FDA, via electronic submission, on January 30, 2003, and confirmation of receipt was received on January 31, 2003 (NDA 021-476);

(c) Sepracor received an Approval Letter from the FDA for LUNESTA™ (eszopiclone) NDA 021-476 on December 15, 2004.

(11) "A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities;" 37 C.F.R. § 1.740(a)(11).

Attached is a chronology that briefly describes the significant regulatory activities and relevant dates associated with Sepracor Inc.'s efforts to seek approval of this product before the FDA (Exhibit B).

(12) "A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of the extension claimed, including how the length of extension was determined;" 37 C.F.R.§ 1.740(a)(12).

Statement of Eligibility of the Patent for Extension

It is the opinion of the Applicant that U.S. Patent No. 6,444,673 is eligible for an extension. This opinion is based on the following information on U.S. Patent No. 6,444,673:

(a) 35 U.S.C. § 156(a): U.S. Patent No. 6,444,673 claims the approved human drug product LUNESTA™ (eszopiclone).

(b) 35 U.S.C. § 156 (a)(1): The term of said patent has not expired prior to the submission of this application.

(c) 35 U.S.C. § 156 (a)(2): The term of said patent has never been previously extended under 35 U.S.C. § 156 (e)(l).

(d) This application for extension is in compliance with 37 C.F.R. § 1.740.

(e) 35 U.S.C. § 156(a)(4): The product, LUNESTA™ (eszopiclone), has been subject to a regulatory review period as defined in 35 U.S.C. § 156(g) before its commercial marketing or use.

(f) 35 U.S.C. § 156(a)(5)(A): The NDA for the product received approval under the provision of law (i.e., FDC Act §505) under which the applicable regulatory review occurred.

(g) This application was submitted within sixty (60) days from the December 15, 2004 NDA approval date.

(h) 35 U.S.C. § 156(c)(4): No other patent term has been extended for the same regulatory review period for this product.

Statement as to Length of Extension Claimed

The term of U.S. Patent No. 6,444,673 should be extended by 760 days (i.e. 2 years 30 days), or until February 14, 2014 (as 2012 is a leap year). This term of extension was determined on the following bases.

First, the following calculation of the regulatory period is in accordance with 35 U.S.C. § 156 and 37 C.F.R. § 1.775. The length of this extension was determined as follows:

The effective date of the Investigational New Drug (IND) application is August 21, 1999, which was thirty (30) days after FDA receipt of the IND on July 22, 1999. The IND number is 58,647.

The new drug application (NDA) for LUNESTA™ was initially submitted via electronic filing to the FDA on January 30, 2003 and receipt was acknowledged by the FDA on January 31, 2003.

An approval letter for the NDA was issued by the FDA on December 15, 2004.

U.S. Patent No. 6,444,673 issued on September 3, 2002, and is entitled to a patent term of 20 years from the earliest filing date (January 16, 1992).

As set forth in 35 U.S.C. § 156(g)(1)(B), the regulatory review period for a new drug equals the sum of the following periods (i) and (ii):

(i) The time between the date an exemption under §505(i) of the FFDCA became effective (the effective date of the IND) and the date an application was initially submitted under §505 of the FFDCA (the date of the initial submission of the NDA).

An IND for the product was effective on August 21, 1999. The NDA for the product was submitted on January 30, 2003. Thus, for the purpose of this calculation, item (i) for the product equals the number of days from August 21, 1999, to January 30, 2003, or 1258 days.

(ii) The time between the date an application was initially submitted under §505(b) of the FFDCA (the date of the initial submission of the NDA) and the date the application was approved (the approval date of the NDA).

The NDA for the product was submitted on January 30, 2003. The NDA was approved on December 15, 2004. Thus, for the purpose of this calculation, item (ii) equals the number of days from January 30, 2003, to December 15, 2004, or 685 days.

In accordance with 35 U.S.C. § 156(c), the term of a patent eligible for extension shall be extended by the time equal to the regulatory review period for the approved product which occurred after the date the patent issued. U.S. Patent No. 6,444,673 issued on September 2, 2002. For the portion of the regulatory review period calculated pursuant to item (i) above, the period occurring after issuance of the patent equals the number of days from September 2, 2002 to January 30, 2003, or 150 days. The entire regulatory review period calculated for item (ii) above occurred after the issuance date of the patent.

Second, 35 U.S.C. § 156(c)(1)-(3) also set forth the following exceptions which may operate to reduce the length of the review period used to calculate patent term extension.

(1) Each period is reduced by any period during which the applicant did not act with due diligence.

There has been no lack of due diligence during the period of regulatory review.

Accordingly, no reduction in the review period is required by this provision.

(2) Each period includes only one-half of the number of days in phase (i).

One-half of the number of days in phase (i) equals one-half of 150 days, or 75 days. Adding this number of days to the number of days in phase (ii) (685 days) results in a review period of 760 days.

(3) If the period remaining in the patent term after the date of approval of the approved product when added to the regulatory review period as revised under paragraphs (1) and (2) above exceeds fourteen years, the period of extension shall be reduced so that the sum of both such periods does not exceed fourteen years.

On the date of approval of the NDA for the product, December 15, 2004, 9 years and 146 days remained in the term of U.S. Patent No. 6,444,673. Adding this period to the review period calculated above yields a period of less than fourteen years. This provision, therefore, does not affect the period of extension to which U.S. Patent No. 6,444,673 is entitled.

Third, 35 U.S.C. §156(g)(6) limits the period of patent term extension to a maximum of five years from the original expiration date of the patent. The original expiration date of U.S. Patent No. 6,444,673 is January 16, 2012. Accordingly, the maximum extension allowed by this provision would extend the term to January 16, 2017. Extension of the patent by the number of days calculated above would not extend the patent beyond this date. Accordingly, this provision does not operate to shorten the period of extension to which U.S. Patent No. 6,444,673 is entitled.

Thus, U.S. Patent No. 6,444,673 is entitled to an extension of 760 days (i.e. 2 years and 30 days), to February 14, 2014.

(13) "A statement that applicant acknowledges a duty to disclose to the Director of the United States Patent and Trademark Office and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought;" 37 C.F.R. § 1.740(a)(13).

Applicant acknowledges a duty to disclose to the Director of the United States Patent and Trademark Office and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to any determination of entitlement to the extension sought.

(14) "The prescribed fee for receiving and acting upon the application for extension (see §1.20(j));" 37 C.F.R.§ 1.740(a)(14).

Pursuant to 37 C.F.R. § 1.20(j), a check in the amount of $1,120.00 is enclosed with this application.

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Director is hereby authorized to charge Deposit Account No. 08-1935 for any such fees. Should a refund of fee paid be necessary, the Director is hereby authorized to credit any such amount to Deposit Account No. 08-1935.

(15) "The name, address and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed;" 37 C.F.R.§ 1.740(a)(15).

Please direct all inquiries and correspondence relating to this application for term extension to:

Philip E. Hansen
HESLIN ROTHENBERG FARLEY & MESITI, P.C.
5 Columbia Circle
Albany, New York 12203-5160
Telephone: (518) 452-5600
Facsimile: (518) 452-5579

(16) "The application under this section must be accompanied by two additional copies of such application (for a total of three copies)." 37 C.F.R.§ 1.740(b).

This application for patent extension, including its attachments, is being submitted as one original and two duplicate copies thereof.

Respectfully submitted,

February 11, 2005
Date

Philip E. Hansen
Agent for Applicants
Reg. No. 32,700

VENABLE LLP

575 7th Street, NW
Washington, DC 20004-1601

Telephone 202-344-4000
Facsimile 202-344-8300

www.venable.com

David G. Adams (202) 344-8014 dgadams@venable.com

December 30, 2005

VIA FEDERAL EXPRESS

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

Re: Citizen Petition re Date of Approval for Lunesta™ (Eszopiclone) Tablets

Dear Sir or Madam:

Please accept the attached petition and exhibits (in four copies) submitted on behalf of Sepracor Inc. pursuant to 21 C.F.R. § 10.35.

Sincerely,

David G. Adams

302

500

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* Call for Confirmation:

5 Packaging * Declared value limit $500.

- [ ] FedEx Envelope*
- [x] FedEx Pak* — Includes FedEx Small Pak, FedEx Large Pak, and FedEx Sturdy Pak.
- [ ] FedEx Box
- [ ] FedEx Tube
- [ ] Other

6 Special Handling Include FedEx address in Section 3.

- [ ] **SATURDAY Delivery** — Available ONLY for FedEx Priority Overnight, FedEx 2Day, FedEx 1Day Freight, and FedEx 2Day Freight to select ZIP codes.
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- [ ] **HOLD Saturday at FedEx Location** — Available ONLY for FedEx Priority Overnight and FedEx 2Day to select locations.

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		Credit Card Auth.

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- [ ] Direct Signature — Anyone at recipient's address may sign for delivery. *Fee applies.*
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