DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 078179

Actavis South Atlantic LLC
Attention: Monique Weitz
Senior Director, Regulatory Affairs
13800 N.W. 2nd Street, Suite 190
Sunrise, FL 33325

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated February 22, 2006, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg and 12.5 mg.

Reference is also made to your amendments dated February 24, April 10, April 11, July 24, October 4, October 23, and December 5, 2006; January 30, 2007; April 7, May 7, June 19, August 13, October 23, and December 1, 2009; and February 25, February 26, May 20, June 15, July 20, July 21, and August 13, 2010. Reference is also made to your correspondence dated May 17, and June 13, 2006; and February 13, and March 27, 2007, addressing the patent issues associated with this ANDA.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg, at this time because of the exclusivity issue noted below. Therefore, only your Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg is **approved**. Your Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg is **tentatively approved**.

The reference listed drug (RLD) upon which you have based your ANDA, Ambien CR Extended-release Tablets of Sanofi Aventis US, LLC. (Sanofi), is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"),

U.S. Patent No. 6,514,531 (the '531 patent) is scheduled to expire on June 1, 2020 (with pediatric exclusivity added).

Your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '531 patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg and 12.5 mg, under this ANDA. You have notified the agency that Activis complied with the requirements of section 505(j)(2)(B) of the Act, and that no action for infringement was brought against Actavis within the statutory 45-day period, which action would have resulted in a 30-month stay of approval under section 505(j)(5)(B)(iii).

I. Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg (Original #1)

With respect to your Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg, we have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, your Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg, is **approved**, effective on the date of this letter. The Division of Bioequivalence has determined your Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg, to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Ambien CR Extended-release Tablets, 6.25 mg, of Sanofi Aventis US, LLC. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows:

Dissolution Testing should be conducted in 500 mL of 0.01N HCl at 37°C using USP apparatus I (Basket) at 100 rpm. The test product should meet the following "interim" dissolution specifications:

Time (Hours)	Percent Dissolved
0.5	(b) (4)
1.5	NLT (b) (4)
4	NLT (b) (4)

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the

final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

With respect to 180-day generic drug exclusivity, the agency has concluded that Actavis was the first ANDA applicant to submit a substantially complete ANDA for Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg, with a paragraph IV certification to the '531 patent. The agency notes that Actavis failed to obtain tentative approval of this ANDA within 30 months after the date on which the ANDA was filed. We have determined, however, that this was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed. Therefore, with this approval, the agency has determined that Actavis is eligible for 180 days of generic drug exclusivity for Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Within 10 days of commercial marketing, please submit correspondence to this ANDA informing the agency of the date you begin commercial marketing of Zolpidem Tartrate Extended-release Tablets USP, 6.25 mg. Please also be aware that, if an event described in section 505(j)(5)(D) occurs, exclusivity shall be forfeited.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

II. Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg (Original #2)

As noted above, your Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg, is **tentatively approved**. Prior to the submission of your ANDA, another applicant submitted an ANDA providing for Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg, and containing a paragraph IV certification to the '531 patent. Your ANDA will be eligible for final approval on the date that is 180 days after the date the agency receives notice, with respect to the other ANDA, of the commercial marketing date identified in section 505(j)(5)(B)(iv) of the Act, or the 180-day generic drug exclusivity of the other applicant is otherwise resolved.

To reactivate your ANDA prior to final approval of the 12.5 mg strength, please submit a "***MINOR AMENDMENT TO ORIGINAL #2 - FINAL APPROVAL REQUESTED***" 90 days prior to the date you believe that your Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg, will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, if appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a ***MINOR AMENDMENT TO ORIGINAL #2 - FINAL APPROVAL REQUESTED***.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either "major" or "minor" changes to **Original #2**, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

Your Zolpidem Tartrate Extended-release Tablets USP, 12.5 mg, may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

For further information on the status of this application, or prior to submitting additional amendments, please contact Benjamin Danso, Pharm.D, Project Manager, at (240) 276-8527.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST

10/13/2010

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.