# CENTER FOR DRUG EVALUATION AND RESEARCH

# APPLICATION NUMBER:

# 76-168

# TENTATIVE APPROVAL LETTER(S)

ANDA 76-168

SEP 29 2003

TEVA Pharmaceuticals USA
Attention: Philip Erickson
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated May 8, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Oxycodone Hydrochloride Extended-release Tablets, 80 mg.

Reference is also made to your amendments dated May 5, and July 2, 2003. We also refer to your communications dated August 3, and November 15, 2001, addressing patent issues noted below.

We have completed the review of this abbreviated application 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 application at this time due to the ongoing patent litigation issues explained below. Therefore, the application is **tentatively approved.** This determination is based upon information available to the agency at this time (i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address notice issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The listed drug product (RLD) referenced in your application, OxyContin Controlled-release Tablets, 80 mg, of Purdue Pharma LP, is subject to multiple periods of patent protection. As noted in the agency's publication entitled Approved Drug

Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. patents 4,861,598 (the '598 patent), and 4,970,075 (the '075 patent) are scheduled to expire on August 29, 2006; U.S. patents 5,266,331 (the '331 patent), 5,549,912 (the '912 patent), and 5,656,295 (the '295 patent) are scheduled to expire on October 26, 2007; and U.S. patent 5,508,042 (the '042 patent) is scheduled to expire on April 16, 2013. Your application contains a paragraph IV certification to each of these patents under Section 505(j)(2)(A)(IV) of the Act stating the patents are invalid, unenforceable, and that your manufacture, use, or sale of Oxycodone Hydrochloride Extended-release Tablets, 80 mg, will not infringe on any of these patents. Section 505(j)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action is brought against TEVA Pharmaceuticals USA (TEVA) for infringement of one or more of the patents which were the subjects of the paragraph IV certifications. This action must be brought against TEVA prior to the expiration of forty-five (45) days from the date the notice TEVA provided under paragraph (2)(B)(i) was received by the NDA/patent holder(s). You notified the agency that TEVA complied with the requirements of Section 505(j)(2)(B) of the Act. As a result, patent infringement actions were filed against TEVA involving challenges to the '912, '042, and '295 patents. Litigation involving these three patents is currently underway in the United States District Court for the Southern District of New York (Purdue Pharma L.P., The Purdue Frederick Company, The P.F. Laboratories, Inc., The Purdue Pharma Company, v. TEVA Pharmaceuticals USA, Inc., Civil Action No. 01-CV-8507). Therefore, final approval for this ANDA cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) since the date of receipt of the 45-day notice required under section 505(j)(2)(B)(i), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or,

   b. the date of a court decision on the contested patents [505(j)(5)(B)(iii) (I), (II), or (III)], or

   c. all listed patents have expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

In order to reactivate this application prior to final approval, please submit a MINOR AMENDMENT - FINAL APPROVAL REQUESTED 90 days prior to the date you believe the application will be eligible for final approval. This amendment should include a justification for why you believe the application should be approved including, if necessary:

1. A copy of a final order or judgement, settlement agreement between the parties, licensing agreement between you and the patent holder, or any other relevant information, and

2. a. updated information related to labeling or chemistry, manufacturing and controls data, or any other change in the conditions outlined in this abbreviated application, or

   b. a statement that no such changes have been made to the application since the date of tentative approval.

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

Any significant changes in the conditions outlined in this abbreviated application 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, and they will be reviewed according to OGD policy in effect at the time of their receipt. The submission of multiple amendments prior to approval may also result in a delay in the issuance of the final approval letter.

This drug product 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 before the effective final approval date is prohibited under

section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be listed in the "Orange Book."

For further information on the status of this application, or prior to your submission of additional amendments, please contact Ted Palat, Pharm.D., Project Manager, at 301-594-0338, for further instructions.

Sincerely yours,

Gary Buehler 9/29/03
Director
Office of Generic Drugs
Center for Drug Evaluation and Research