CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-278

TENTATIVE APPROVAL LETTERS

ANDA 75-278

SEP 19 2000

Mylan Pharmaceuticals, Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

Dear Sir:

This is in reference to your abbreviated new drug application dated December 19, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Paclitaxel Injection, 30 mg/5mL (6 mg/mL).

Reference is also made to your amendments dated August 26, 1998, January 13, May 5, May 12, July 25, and September 15, 2000.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. 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), and 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 referenced in your application, Taxol Injection of Bristol Myers Squibb Co. Pharmaceutical Research Institute, is subject to a period of patent protection which expires on August 3, 2012, (U.S. Patent No. 5,641,803 [the '803 patent] and U.S. Patent No. 5,670,537 [the '537 patent]). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of Paclitaxel Injection will not infringe on the '803 or '537 patents. Your application also contains a patent statement under Section 505(j)(2)(A)(viii) of the Act indicating that U.S. Patent No. 5,496,804 [the '804 patent] is a method of use patent, and that this patent does not claim any of the

proposed indications for which you are seeking approval. You have informed the Agency that Mylan Pharmaceuticals, Inc. has complied with the requirements of Section 505(j)(2)(B) of the Act and that Bristol Myers Squibb Co. Pharmaceutical Research Institute initiated a patent infringement suit against you in the United States District Court for the District of New Jersey with respect to the '803 and '537 patents (Bristol Myers Squibb Company v. Mylan Pharmaceuticals, Inc., Civil Action No. 98-1488). The Agency recognizes that the 30-month period identified in Section 505(j)(5)(iii) of the Act, during which time FDA was precluded from approving your application, has expired.

Please note that an abbreviated application for Paclitaxel Injection, 6 mg/mL, containing a Paragraph IV Patent Certification was accepted for filing by this Office prior to the filing of your application. This application, submitted by Baker Norton Pharmaceuticals, Inc., received final approval on September 15, 2000. Consequently, Baker Norton Pharmaceuticals is eligible for 180-days of generic drug market exclusivity. Your application will be eligible for final approval beginning one hundred and eighty (180) days after the first commercial marketing of the drug by Baker Norton Pharmaceuticals, Inc. We refer you to the Agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998), for additional information.

Because the Agency is granting a tentative approval for this application, please submit an amendment at least 60-days but not more that 90-days prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the drug product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing and controls data as appropriate. Alternatively, an amendment should be submitted stating that no changes have been made to the terms of the application since the date of tentative approval. This submission should be designated clearly in your cover letter as a MINOR amendment. In addition to, or instead of, the amendment requested above, the Agency may, at any time prior to the final date of approval, request that you submit an amendment containing the information described above.

Any changes in the conditions outlined in this abbreviated application and the status of the manufacturing and testing facilities' compliance with current good manufacturing procedures are subject to Agency review before final approval of the application will be made.

In addition to, or instead of, the amendments referred to above, the Agency may, at any time prior to the final date of approval, request that you submit amendments containing the information requested above.

Failure to submit either or both amendments may result in rescission of this tentative approval determination, or delay in issuance of the final approval letter.

The drug product that is the subject of this abbreviated application 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. Also, until the Agency issues the final approval letter, this drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list.

The amendment should be designated as a MINOR AMENDMENT in your cover letter. Before you submit the amendment, please contact Michelle Dillahunt, Project Manager, at (301) 827-5848, for further instructions.

The introduction or delivery for introduction into interstate commerce of the drug before the effective approval ate is prohibited under 21 U.S.C. 331(d).

Sincerely yours,

/S/

Gary Buehler 9/19/00
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-278

JAN 25 2002

Mylan Pharmaceuticals, Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

Sent by Facsimile and U.S. Mail

Dear Mr. Sisto:

This is in reference to your abbreviated new drug application (ANDA) for Paclitaxel Injection, 6 mg/mL, packaged in 30 mg/5 mL, 100 mg/16.7 mL, and 300 mg/50 mL multiple-dose vials, dated December 19, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act (Act). This letter is to inform you that, in light of the January 24, 2002, Order entered by Judge Colleen Kollar-Kotelly in *ABI v. Thompson*, Civil Action No. 02247 (CKK), in the U.S. District Court for the District of Columbia (Order), the final approval given to Mylan Pharmaceuticals, Inc. on July 23, 2001, for this application, including all amendments and supplements thereto, is hereby rescinded.

The January 24, 2002 Order is attached. It is based upon a finding that U.S. Patent No. 6,096,331 was timely filed under section 505(c)(2) of the Act at the time your ANDA was approved. Because, at that time, ANDA 75-278 did not contain a patent certification as required by section 505(j)(2)(A)(vii) of the Act, it did not meet the statutory standard for approval. Therefore, pursuant to the Order, the Agency finds that the final approval for this application, including all amendments and supplements thereto, is rescinded.

The Agency notes, that based upon the information you have presented to date, the drug described in your ANDA is safe and effective for use as recommended in the submitted labeling. 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 products, and is subject to change on the basis of new information that may come to our attention.

The listed drug product referenced in your application (RLD), Taxol® Injection of Bristol Myers Squibb Co. Pharmaceutical Research Institute, is subject to periods of patent protection which expire on August 3, 2012, [U.S. Patent No. 5,641,803 (the '803 patent), and U.S. Patent No. 5,670,537 (the '537 patent)]; May 08, 2011[U.S. Patent No. 6150398 (the '398 patent)]; and March 9, 2013 [U.S. Patent No. 5,496,804 (the '804 patent)]. Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of Paclitaxel Injection will not infringe on the '803 or '537 patents. Your application also contains statements under Section 505(j)(2)(A)(viii) of the Act indicating that the '804 patent and the '398 patent are methods of use patents, and that your labeling for paclitaxel injection does not claim the indications or methods of use covered by these patents. You have informed the Agency that Mylan Pharmaceuticals, Inc. has complied with the requirements of Section 505(j)(2)(B) of the Act and that Bristol Myers Squibb Co. Pharmaceutical Research Institute initiated a patent infringement suit against you in the United States District Court for the District of New Jersey with respect to the '803 and '537 patents (Bristol Myers Squibb Company v. Mylan Pharmaceuticals, Inc., Civil Action No. 98-1488). The Agency recognizes that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application, has expired.

Taxol® is also covered by periods of Waxman-Hatch exclusivity, D-57, I-270, I-226 and I-230; and Orphan Drug Exclusivity (ODE) that are listed in Approved Drug Products with Therapeutic Equivalence Evaluations, 21st Edition (Orange Book). You have made a statement that your labeling for paclitaxel injection does not claim the indications or methods of use covered by such exclusivity.

Please note that on January 17, 2002, Bristol Myers Squibb withdrew the listing of U.S. Patent No. 6,096,331. This patent is no longer listed in the Orange Book for Taxol®, the RLD identified in your ANDA. Therefore, you are not required to submit a certification under section 505(j)(2)(A)(vii) of the Act for this patent.

Because the Agency is granting a **tentative approval** for this application, when you believe that your application may be considered for final approval, you must amend your application to notify the Agency whether circumstances have or have not arisen that may affect the effective date of final approval. To reactivate your application, please submit an amendment prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing, and controls data as appropriate. Please note that this amendment should be submitted even if none of these changes were made. The amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above. Any 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 procedures are subject to Agency review before final approval of the application will be made.

The drug products that are the subject of this abbreviated application may not be marketed without final Agency approval under section 505 of the Act. The introduction or delivery or introduction into interstate commerce of this drug before the effective final approval date is prohibited under section 301(d) of the Act. Also, until the Agency issues the final approval letter, these drug products will not be listed in the Orange Book.

Please contact Cecelia Parise, R.Ph., Regulatory Policy Advisor to the Director, Office of Generic Drugs, at (301) 827-5845, for further information regarding this issue.

Sincerely yours,

/S/

Gary J. Buehler 1/25/02
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL