

December 29, 1998

Bedford Laboratories
A Division of Ben Venue Laboratories, Inc.
Attention: Shahid Ahmed
300 Northfield Road
Bedford, OH 44146

Dear Sir:

This is in reference to your abbreviated new drug application dated December 23, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Cisplatin Injection 1 mg/mL, 50 mL/vial and 100 mL/vial.

Reference is also made to your amendments dated March 4 and 24, 1997; and April 13, October 22, and December 10, 1998.

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 manufacturing 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 is subject to periods of patent protection which expire on January 12, 1999, (Patent No. 4,310,515, the '515 patent) and May 8, 2012, (Patent No. 5,562,925, the '925 patent). Your application contains certifications to each of these patents under Section 505(j)(2)(A)(vii)(IV) of the Act stating that to the best of Bedford Laboratories' knowledge, the '515 patent will not be infringed by the manufacture, use, or sale of this drug product and that the '925 patent is invalid. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement or to contest the validity of the patent(s) which are the subject of the certifications before the expiration of forty-five days from

the date the notice provided under paragraph (2)(B)(I) is received. However, you have notified the Agency that litigation is underway in the United States District Court for the Northern District of Ohio, Eastern Division involving a challenge to the '925 patent (Research Corporation Technologies, Inc. and Bristol-Myers Squibb Company v. Ben Venue Laboratories, Inc., [Civil Action No. 1:97CV00872]). Therefore, final approval 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 court decision [505(j)(5)(B)(iii) (I), (II), or (III)], which has been interpreted by the Agency to mean the date of the final order or judgement of that court from which no appeal can be or has been taken, or,
 - c. the '925 patent has expired, and
2. The Agency is assured there is no new information that would affect whether final approval should be granted. In addition, the 180-day exclusivity provisions for this drug product under Section 505(j)(5)(B)(iv) must be satisfactorily addressed.

Because the Agency is granting a tentative approval for this application, when you believe that your application should be considered for final approval, you must amend your application to notify the Agency of the circumstances that may affect the effective date of final approval. Your amendment must provide:

1. a copy of a final order or judgement from which no appeal may be taken (which might not be the one from the district court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information, and
2. a. updated information related to final-printed labeling or chemistry, manufacturing and controls data, or any other change in the conditions contained in this abbreviated application, or
- b. a statement that no such changes have been made to

the application since the date of tentative approval.

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 cover letter accompanying your amendment submitted in response to this tentative approval letter to request final approval of this ANDA should clearly emphasize that the amendment is intended to represent a MINOR AMENDMENT. Before you submit the amendment, please contact Denise Huie, Project Manager, at (301) 827-5848, for further instructions.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research