ANDA 74-253 March 28, 2001

Danbury Pharmacal, Inc.
Attention: Ernest Lengle, Ph.D.
311 Bonnie Circle
Corona, CA 92878-1900

Dear Sir:

This is in reference to your abbreviated new drug application dated July 31, 1992, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Buspirone Hydrochloride Tablets USP, 5 mg, 10 mg, and 15 mg.

Reference is also made to your amendments dated December 8, December 16, and December 24, 1992; January 20, March 1, and March 18, 1993; March 17, (2 submissions), November 7, and November 20, 2000; and February 8, March 8, March 13, and March 28, 2001. We note that your November 7, 2000, amendment effects the transfer of data from Chelsea Laboratories Inc's. (Chelsea) ANDA 75-195 into this application. Both Chelsea and Danbury Pharmacal, Inc. are wholly owned subsidiaries of Watson Pharmaceuticals, Inc.

The listed drug product (RLD) referenced in your application, BuSpar® Tablets of Bristol Myers Squibb Co. Pharmaceutical Research Institute (BMS), is subject to a period of patent protection which expires on November 14, 2008 (U.S. Patent No. 5,015,646 [the '646 patent]). Your application contains a Paragraph IV Certification to the '646 patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe on this patent or that the patent is otherwise invalid. You have further notified the Agency that Danbury Pharmacal, Inc. (Danbury) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no legal action regarding the '646 patent was brought against Danbury within the statutory forty-five day period.

We note that Danbury also made a Paragraph IV Certification to U.S. Patent No. 6,150,365 (the "365 patent"). However, as a result of recent litigation, Bristol-Myers Squibb Company

(BMS), the holder of the NDA for Buspar, requested the agency to remove the '365 patent from the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). In response to this request, as of March 28, 2001, the '365 patent is no longer considered to be listed in the Orange Book. Thus, you are not required to submit a certification to this patent. Your amendment dated March 28, 2001, provides for the withdrawal of your certification to the '365 patent.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug product is safe and effective for use as recommended in the submitted labeling. However, because of the unique (split) generic drug exclusivity issues associated with this drug product, the Agency is unable to approve all three strengths of the drug product. **Accordingly, only the 5 mg and 10 mg strengths of the drug product are approved at this time. The 15 mg strength shall be tentatively approved** and will not receive final approval until the remaining exclusivity issues are satisfactorily resolved. The Division of Bioequivalence has determined your Buspirone Hydrochloride Tablets USP, 5 mg and 10 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Buspar Tablets, 5 mg and 10 mg, respectively, of Bristol Myers Squibb Co. Pharmaceutical Research Institute). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

With respect to 180-day generic drug exclusivity, we note that Danbury was the first applicant to submit a substantially complete ANDA with a Paragraph IV Certification for the 5 mg and 10 mg strengths only. Therefore, with this approval Danbury is eligible for 180-days of market exclusivity for the 5 mg and 10 mg strengths. Such exclusivity will begin to run from the date Danbury begins commercial marketing of the 5 mg and 10 mg strengths. With respect to the "first commercial marketing" trigger for the commencement of exclusivity, please refer to 21 CFR 314.107(c)(4). The Agency expects that you will begin commercial marketing of both of the 5 mg and 10 mg strengths of this drug product in a prompt manner.

If you have questions concerning the effective date of approval of an abbreviated new drug application and the

Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

We are unable to grant final approval to the 15 mg strength at this time because an abbreviated application for Buspirone Hydrochloride Tablets, USP containing a Paragraph IV Certification for the 15 mg strength was accepted for filing by OGD prior to its receipt of your application containing a similar certification. Accordingly, the 15 mg strength provided for in your application will be eligible for final approval beginning on the date that is one hundred and eighty days after the date the Agency receives notice of the first commercial marketing of the 15 mg strength under the prior application. We refer you to the Agency's recently issued guidance document "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998), for additional information.

Under section 505(A) of the Act, certain changes in the conditions described in this abbreviated application for the 5 mg and 10 mg strengths require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application as applied to the approved 5 mg and 10 mg strengths are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of these approved strengths of Buspirone Hydrochloride Tablets, USP.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and

Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Our decision to grant tentative approval status to the 15 mg strength of this drug product 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 decision is subject to change on the basis of new information that may come to our attention.

To provide for final approval of the 15 mg strength, please submit a supplemental application as directed below. The Agency will provide written notice of the information needed to determine the earliest possible final approval date of your supplemental application for the 15 mg strength under section 505(j)(5)(B)(iv) as soon as such information becomes available. The supplemental application, which must be submitted for prior approval at least 60 days prior to the date you believe the 15 mg strength will be eligible for final approval, should include updated information such as final-printed labeling, and chemistry, manufacturing and controls data as appropriate. Alternatively, a prior approval supplement should be submitted to request final approval of the 15 mg strength and stating that no changes have been made to the application since the date of this letter. Because of the unique circumstances associated with exclusivity for this drug product, the office will entertain your request that the supplemental application be granted “expedited review” status.

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 supplemental application will be made.

In addition to, or instead of the supplemental application requesting final approval of the 15 mg strength, the Agency may at any time prior to final approval, request that you submit an informational document containing the information

stated above.

Failure to submit the supplemental application or informational document may result in rescission of the tentative approval determination, or delay in issuance of the final approval letter for the 15 mg strength.

The 15 mg strength of Buspirone Hydrochloride Tablets, USP may not be marketed without final Agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of these unapproved strengths before the final approval date is prohibited under section 501 of the Act. Also, until the Agency issues the final approval letter, these three additional strengths of the drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the “Orange Book”).

Should you have any questions about the approval status of the various strengths of drug product presented in your application, or about the timing or content of the supplemental application to provide for final approval of the remaining strengths, please contact Ms. Elaine Hu, R.Ph., Project Manager, at
(301) 827-5848.

Sincerely yours,

Gary Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research