ANDA 75-467 March 28, 2001

Par Pharmaceutical, Inc.
Attention: Michelle Bonomi-Huvala
One Ram Ridge Road
Spring Valley, NY 10977

Dear Sir:

This is in reference to your abbreviated new drug application dated September 29, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Buspirone Hydrochloride Tablets USP, 5 mg, 7.5 mg, 10 mg, and 15 mg.

The inclusion of the 7.5 mg strength of this drug product is based upon an approved ANDA Suitability Petition submitted under Section 505(j)(2)(C) of the Act.

Reference is made to our letters dated December 28, 1999 and May 23, 2000, granting tentative approval to this drug product. Reference is also made to your amendments dated November 9, December 9, and December 18, 1998; February 11, 1999; and
March 14, and March 28, 2001.

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 Par Pharmaceutical, Inc. (Par) 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 Par within the statutory forty-five day period.

We note that Par 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. Please note that because of the unique (split) generic drug exclusivity issues associated with this drug product, the Agency is unable to approve all four strengths of the drug product. **Accordingly, only the 7.5 mg strength of the drug product is approved at this time. The 5 mg, 10 mg, and 15 mg strengths shall remain 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, 7.5 mg, can be expected to have the same therapeutic effect as that of the listed product upon which the Agency relied as the basis of safety and effectiveness. 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 and its impact on the approvability of the remaining strengths presented in this application, we note that Par was the first applicant to submit a substantially complete ANDA with a Paragraph IV Certification only for the 7.5 mg strength. Therefore, with this approval Par is eligible for 180-days of market exclusivity for the 7.5 mg strength. Such exclusivity will begin to run from the date Par begins commercial marketing of the 7.5 mg strength. 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 the 7.5 mg strength 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 5 mg, 10 mg, and 15 mg strengths at this time because abbreviated applications for Buspirone Hydrochloride Tablets, USP containing Paragraph IV Certifications for one or more of these strengths were accepted for filing by OGD prior to its receipt of your application. Accordingly, the 5 mg, 10 mg, and 15 mg strengths 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 one or more of these strengths, respectively, under the prior applications. 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 7.5 mg strength require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for the 7.5 mg strength 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 the 7.5 mg strength 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.

With respect to the continuation of the tentative approval status of the 5 mg, 10 mg, and 15 mg strengths of this drug product, our decision 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 5 mg, 10 mg, and 15 mg strengths, please submit a supplemental application as directed below. Upon request, the Agency will provide written notice of the information needed to determine the earliest possible final approval date of your supplemental application for these three additional strengths under section 505(j)(5)(B)(iv) as soon as such information becomes available. The supplemental application, which must be submitted for prior approval about 60 days prior to the date you believe these strengths 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 these strengths 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 additional strengths, 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 5 mg, 10 mg, and 15 mg strengths.

The 5 mg, 10 mg, and 15 mg strengths 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