CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-140

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-140

NDA APPROVAL

Spectrum Pharmaceuticals, Inc.
Attention: Cynthia Letizia, MPH, RAC
Vice President, Regulatory Affairs
157 Technology Dr.
Irvine, CA 92618

Dear Ms. Letizia:

Please refer to your new drug application (NDA) dated December 14, 1990, received December 18, 1990, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Levoleucovorin for Injection.

We acknowledge receipt of your submissions dated July 10, August 10, September 27, October 23, November 5, 12, December 12, 2007, January 4, 14, February 4, 6, 12, 16, 27, March 3, 4 and 5, 2008.

The July 10, 2007, submission constituted a complete response to our January 3, 1992, action letter.

This new drug application provides for the use of Levoleucovorin for Injection, 50 mg/10 mL or 10 mg/mL for rescue after high-dose methotrexate therapy in osteosarcoma and to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 20-140."

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission

"**Final Printed Carton and Container Labels for approved NDA 20-140.**" Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

We remind you of your postmarketing study commitment in your submission dated March 3, 2008. This commitment is listed below.

Commitment 1:
You have agreed that the structural identity of the degradation products listed as ——— ——— in the drug product specifications, will be confirmed within six months from the date of approval of the NDA. b(4)

Study Start:	by March 2008
Final Report Submission:	by September 2008

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence.**"

An expiration dating period of 24 months is granted when the drug product is stored as recommended in the labeling. You may extend the expiration dating period upon accrual of real time stability data and report this in the next annual report.

A decision on the acceptability of your proposed trade name will be made by the Division of Medication Error Prevention and will be communicated to you at a later date. Accordingly, you may submit a post-approval labeling supplement with inclusion of the accepted trade name. Until then, you may not use any trade name on the labels and labeling, but may only use the established name.

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any question, call Paul Zimmerman, Regulatory Project Manager, at 301-796-1489.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, M.D.
Deputy Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Ann Farrell
3/7/2008 03:51:56 PM