DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-038/S-031

Bayer HealthCare Pharmaceuticals, Inc.
Attention: Dalena DeGrezia
Manager, Global Regulatory Affairs
P.O. Box 1000
Montville, NJ 07045-1000

Dear Ms. DeGrezia:

Please refer to your supplemental new drug application dated June 1, 2007, received June 4, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fludara® (fludarabine phosphate) for Injection.

This "Changes Being Effected" supplemental new drug application provides for revisions to include safety information from post-marketing surveillance.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions indicated below and in the enclosed labeling.

1. **PRECAUTIONS section, Drug Interactions subsection: the following statement is deleted:**

2. **NERVOUS SYSTEM section: the following is added:**

   In post-marketing experience, cases of progressive multifocal leukoencephalopathy have been reported. Most cases had a fatal outcome. Many of these cases were confounded by prior and/or concurrent chemotherapy. The time to onset has ranged from a few weeks to approximately one year after initiating treatment.

3. **REFERENCES:**

   Please update this section to include only the four current references for safe handling.

The final printed labeling (FPL) must be identical to the enclosed labeling, and include the minor editorial revision indicated.

Please submit an electronic version of the FPL according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format - NDA. Alternatively, you may submit 20 paper copies

of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "FPL for approved supplement NDA 20-038/S031." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit revised 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.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division, the Division of Drug Oncology Products, and two copies of both the promotional materials and the package insert directly 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

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

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
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 questions, call Nicholette Hemingway, Regulatory Project Manager, at (301) 796-1365.

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 (labeling with tracked changes)

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

12/20/2007 08:28:23 AM