DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-704/S-008

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Attention: Ellen Wallace, Ph.D.
Associate Director, Regulatory Affairs

Dear Dr. Wallace:

Please refer to your supplemental new drug application dated May 14, 1999, received May 17, 1999, and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DaunoXome® (daunorubicin citrate liposome injection). We note that this application is subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

This "Changes Being Effected" supplemental new drug application provides for safety-related labeling changes to the package insert to strengthen the WARNINGS and ADVERSE REACTIONS sections.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted May 14, 1999). Accordingly, the supplemental application is approved effective on the date of this letter.

However, please note the following minor editorial revisions listed below. These changes should be made at the next printing or within six months, whichever comes first, and noted in the next annual report.

1. According to 21 CFR 201.10 (g)(1), "…If any labeling includes a column with running text containing detailed information as to composition, prescribing, side effects, or contraindications and the proprietary name or designation is used in such column but is not featured above or below the column, the established name shall be used at least once in such column of running text in association with such proprietary name or designation and in the same type size used in such column of running text:…"

   You should either (1) feature the established name and proprietary name or designation above or below each column, or (2) use the established name at least once in each column of running text in association with such proprietary name or designation.

2. In the ADVERSE REACTIONS section, Cardiovascular subsection, add a period at the end of the paragraph.

3. In the DOSAGE AND ADMINISTRATION section, Preparation of Solution subsection, add the letter "s" to the word "tranfer" in the first sentence of the fourth paragraph

4. The "Rx only" phrase should be moved to the TITLE section of the package insert as recommended in the Guidance for Industry Implementation of Section 126 of the Food and Drug Administration Modernization Act of 1997 – Elimination of Certain Labeling Requirements (revised July 1998).

5. You should update the REFERENCES section, as needed, with the references that follow.

1. ONS Clinical Practice Committee. Cancer Chemotherapy Guidelines and Recommendations for Practice. Pittsburgh, Pa: Oncology Nursing Society; 1999:32-41.

2. Recommendations for the Safe Handling of Parenteral Antineoplastic Drugs. Washington, DC: Division of Safety, Clinical Center Pharmacy Department and Cancer Nursing Services, National Institutes of Health; 1992. US Dept of Health and Human Services, Public Health Service Publication NIH 92-2621.

3. AMA Council on Scientific Affairs. Guidelines for Handling Parenteral Antineoplastics. *JAMA*. 1985;253:1590-1591.

4. National Study Commission on Cytotoxic Exposure – Recommendations for Handling Cytotoxic Agents. 1987. Available from Louis P. Jeffrey, Sc.D., Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA 02115.

5. Clinical Oncological Society of Australia. Guidelines and Recommendations for Safe Handling of Antineoplastic Agents. *Med J Australia.* 1983;1:426-428.

6. Jones RB, Frank R, Mass T. Safe Handling of Chemotherapeutic Agents: A Report from the Mount Sinai Medical Center. CA-*A Cancer J for Clin*. 1983;33:258-263.

7. American Society of Hospital Pharmacists. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. *Am J Hosp Pharm.* 1990;47:1033-1049.

8. Controlling Occupational Exposure to Hazardous Drugs. (OSHA Work-Practice Guidelines). *Am J Health-Syst Pharm.* 1996;53-1669-1685.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Dianne Spillman, Regulatory Project Manager, at (301) 594-5746.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Richard Pazdur

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