NDA 21-041 April 1, 1999

DepoTech Corporation
10450 Science Center
San Diego, CA 92121

Attention: Raymond Lamy
Associate Director, Regulatory Affairs

Dear Mr. Lamy:

Please refer to your new drug application (NDA) dated October 2, 1998, received October 5, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DepoCyt® (cytarabine liposomal injection) 10 mg/mL.

We acknowledge receipt of your submissions dated October 2, 5, 6, 15, 23, 26 and 27, 1998; November 3, 4, 5, 6, 12, 13 and 24, 1998; December 3, 4 and 14, 1998; January 12 and 22, 1999; February 3, 5, 19 and 25, 1999; March 24 and 26, 1999.

This new drug application provides for the use of DepoCyt® (cytarabine liposomal injection) 10 mg/mL for the intrathecal treatment of lymphomatous meningitis.

We have completed the review of this application, as amended, according to the regulations for accelerated approval, and have concluded that adequate information has been presented to approve DepoCyt® (cytarabine liposomal injection) 10 mg/mL for use as recommended in the agreed upon labeling text. Accordingly, the application is approved under 21 CFR Subpart H. Approval is effective on the date of this letter. Marketing of this drug product and related activities are to be in accordance with the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-041." Approval of this submission by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your post marketing study (Subpart H Phase 4 commitments) specified in your submissions dated March 25 and 26, 1999. These commitments, along with any completion dates agreed upon, are listed below.

To conduct a Phase 4 Post-Marketing study (Protocol C0101-010) and pharmacokinetic sub-study (C0101-011) titled, "A Randomized Clinical Study to Determine the Patient Benefit and Safety of Depocyt (Cytarabine Liposome Injection) for the Treatment of Solid Tumor Neoplastic and Lymphomatous Meningitis." The studies will be initiated in six months with an interim analysis planned at approximately 4th Quarter 2001. If the study proceeds beyond the interim analysis, the study completion date is estimated to be September 2003.

Final study reports should be submitted to this NDA as a supplemental application. For administrative purposes, all submissions relating to this Phase 4 commitment must be clearly designated "Subpart H Phase 4 Commitments."

As of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until December 2, 2000. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity. However, you should still submit a pediatric drug development plan. We will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

We also remind you that, under 21 CFR 314.550, after the initial 120 day period following this approval, you must submit all promotional materials, including promotional labeling as well as advertisements, at least 30 days prior to the intended time of initial dissemination of the labeling or

initial publication of the advertisement.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when it is available.

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, contact Ann Staten, Project Manager, at (301) 594-5770.

Sincerely,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure