DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 19 1999

WARNING LETTER

Certified Mail-Restricted Delivery
Return Receipt Requested

Ref # HFD-340-0501

Philip B. Gorelick, M.D., M.P.H.
Professor/Director, Stroke Service
Rush-Presbyterian-St. Luke's Medical Center
1645 West Jackson, Suite 400
Chicago, Illinois 60612-3833

Dear Dr. Gorelick:

Between June 4 and 11, 1998, Ms. Sylvia Ayala, representing the Food and Drug Administration (FDA), inspected your conduct as the investigator of record of the following clinical study:

Protocol Number[ ]"Trial of Org 10172 in Acute Stroke Treatment (TOAST)," Orgaran™ (danaparoid sodium) Injection, Sponsored by NIH and Organon, Inc.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects have been protected.

We have evaluated the inspection report, the documents collected during the inspection, and the Inspectional Observations (Form FDA 483) provided to you at the conclusion of the inspection. We find that you significantly violated the Federal Food, Drug, and Cosmetic Act and FDA regulations governing the study of investigational new drugs and the protection of human research subjects in the following respects:

1. You failed to personally conduct or supervise the clinical investigations [21 CFR 312.53 (c)(1)(vi)(c) and 312.60]. This lack of supervision allowed the submission of inaccurate information to the sponsor and FDA in required reports [21 CFR 312.62(b)]. Your study nurse resubmitted to the sponsor stroke logs (i.e., study enrollment logs) which had been altered to indicate a different admission date. The following table summarizes the misrepresented stroke logs.

Date of Original Stroke Log	Date of Altered Stroke Log	Number of Subjects
September 1991	September 1994	18
	March 1996	18
August 1992	February 1995	16
August 1992	January 1995	18
October 1992	January 1995	15
April 1993	April 1995	16
April 1993	April 1995	11
May 1993	May 1995	27

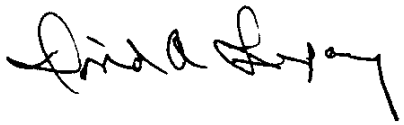
2. You failed to obtain written informed consent for two subjects [21 CFR 50]. There was no documentation to assure that you obtained informed consent from subjects #13 and #32.

Because of the departures from FDA regulations, we request that you notify this office in writing within 15 working days of the corrective actions you have taken, or plan to take to prevent similar violations in the future. Your failure to adequately and promptly correct these matters may result in regulatory action without further notice. If you do not take appropriate action to assure strict adherence to the investigational new drug regulations, we may consider steps that will lead to your disqualification in accordance with 21 CFR 312.70.

If you have any questions, please contact Dr. Antoine El-Hage at (301) 827-1032, FAX (301) 827-5290. Your written response and any pertinent documentation should be addressed to:

Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice II, HFD-344
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, Maryland 20855

Sincerely yours,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research