



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

M333711

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Via Federal Express

• JAN 14 2000

WARNING LETTER

John D. Barr, M.D.
Cleveland Clinic Foundation
Neuroradiology, Hb6
9500 Euclid Avenue
Cleveland, Ohio 44195

Dear Dr. Barr:

During the period of October 18 through October 25, 1999, Joseph L. Despins, Ph.D., an investigator from the Food and Drug Administration's (FDA) Philadelphia District Office visited the Penn State Geisinger Health System, 500 University Drive, Hershey, Pennsylvania. The purpose of Dr. Despins' visit was to determine whether your activities and procedures as a clinical investigator for the [REDACTED] clinical study sponsored by [REDACTED], complied with applicable regulations. This product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

This inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approvals (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of the scientific investigation.

Our review of the inspection report submitted by the Philadelphia District Office revealed significant violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions. These deviations were listed on the Form FDA 483, "Inspectional Observations." Dr. Despins spoke with you via telephone since you are no longer affiliated with the Penn State Geisinger Health System. A copy of the Form FDA 483 was sent to you via Federal Express, by Michael D. O'Meara, Acting Supervisory Investigator, Wilmington Resident Post, Philadelphia District, on October 25, 1999.

The deviations noted on the Form FDA 483 and our subsequent review of the inspection report are summarized below:

Failure to maintain accurate, complete, and current records relating to your participation in an investigational study [21 CFR 812.140(a)(3)].

You failed to maintain accurate, complete, and current records relating to your participation in an investigational study including case report forms (CRFs) and supporting data. For example, a comparison of CRFs and supporting source documentation was performed for ten (10) study subjects who completed the [REDACTED] clinical study at your site. It was determined that the data for all study subjects evaluated showed discrepancies between the source documents and CRFs. The Form FDA 483 (copy enclosed) lists the discrepancies in detail.

In some instances, there is no source documentation to support clinical data entered on CRFs. For example, study subject [REDACTED] did not have source documents for the NIH Stroke Scale (post-resection) and clinical neurological exam (post-resection), although data were reported on the CRFs.

In addition, data recorded on source documents were not accurately reported on CRFs. For example, on Form 9, *Surgery*, for study subject [REDACTED], it states under Number 5, *Comment (record ease of retraction and resection)*: "Difficult Surgery, Time Consuming." Whereas, the Operative Report source document, describes a different and more detailed analysis: "[REDACTED]"

Failure to maintain accurate, complete, and current records relating to device accountability [21 CFR 812.140(a)(2)(ii) and (iii)].

You failed to maintain accurate and complete documentation regarding the disposition of the study device. For example, a portion of the *Device Accountability Log* [REDACTED], shows the number of [REDACTED] received, dispensed, and remaining as follows:

No. [REDACTED] Received	Date Dispensed	Subject ID # Initials	No. [REDACTED] Remaining	Comment
	07/29/98	[REDACTED]	8	1 [REDACTED] [used]
	08/11/98	[REDACTED]	7	1 [REDACTED] used
	09/28/98	[REDACTED]	7	2 [REDACTED] used
	11/10/98	[REDACTED]	6	1 [REDACTED] opened
	11/11/98	[REDACTED]	5	1 [REDACTED] used
	11/13/98	[REDACTED]	3	2 [REDACTED] used
3 (11/16/98)		[REDACTED]	6	3 [REDACTED] received
	11/16/98	[REDACTED]	5	1 [REDACTED] used
			0	Returned 5 [REDACTED]

On 11/16/98 the accountability log shows that "3" [redacted] were received; and "1 [redacted] used" for study subject ID # [redacted], initials [redacted]. At the end of the accountability log there is a comment, "Returned 5 [redacted]". If the disposition of the [redacted] is accurately recorded under the comment section of the accountability log, then the number of [redacted] returned to the sponsor should be three (3) rather than five (5) as recorded in the log. There is no documentation given to explain this discrepancy.

The deviations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a Clinical Investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. To assist you, we have enclosed a copy of the *FDA Information Sheets*, guidance for clinical investigators.

Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter** of the specific steps you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond can result in further regulatory action, including disqualification, without additional notice.

You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kathleen E. Swisher, R.N., J.D., Consumer Safety Officer.

A copy of this letter has been sent to our Philadelphia District Office, U.S. Custom House, Room 900, 2nd and Chestnut Streets, Philadelphia, Pennsylvania 19106. We request that a copy of your response be sent to that office as well.

Sincerely yours,



Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosures