



Via Federal Express

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Warning Letter

• JUL 25 2003

Barry S. George, M.D.
MidWest Cardiology Research Foundation
3545 Olentangy River Road, Suite 220
Columbus, Ohio 43214

Dear Dr. George:

The purpose of this letter is to inform you of the objectionable conditions found during a Food and Drug Administration (FDA) inspection at your clinical site and to request a reply. Mr. Hugh M. McClure III of the Cincinnati District Office conducted the inspection on March 12-24, 2003.

The purpose of the inspection was to determine whether your activities as a clinical investigator in the study entitled [REDACTED]

[REDACTED] complied with applicable FDA regulations. The purpose of the clinical trial was to evaluate a new delivery system for the [REDACTED]. The [REDACTED] is a device as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(h)].

The inspection was conducted under an FDA compliance program designed to ensure that data and information contained in requests for Investigational Device Exemption (IDEs), Premarket Approval Applications (PMAs), and Premarket Notification submissions (510(k)s) 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 scientific investigations. The aforementioned study was conducted under [REDACTED]

Our review of the establishment inspection report prepared by the Cincinnati District Office reveals violations of the requirements of Title 21, Code of Federal Regulations (CFR), Part 812 – Investigational Device Exemptions. At the conclusion of the inspection, Mr. McClure listed his findings on a Form FDA-483 “Inspectional Observations,” and discussed these findings with [REDACTED], on your behalf. [REDACTED] were also present at this meeting.

In an April 3, 2003, letter, [REDACTED], on your behalf, acknowledged the FDA-483 items. His response to the FDA-483 is inadequate in that it does not contain a corrective action plan with specific times for completion and supporting documentation for corrections already made.

FDA considers your violations to be of particular concern because we observed similar protocol deviations during an inspection of the [REDACTED] conducted from January 24-February 8, 2001. In a February 12, 2001, letter to FDA, you promised to correct the noted deficiencies and to comply with FDA regulations. Despite those assurances, the current inspection revealed continuing deficiencies with respect to your following the investigation's protocol requirements.

The violations in the [REDACTED] study noted on the FDA-483 and evident from our subsequent review of the inspection report are summarized below.

Failure to conduct an investigation in accordance with the investigational plan (21 CFR Part 812.110(b))

You failed to enroll subjects according to the inclusion/exclusion criteria. For example, you enrolled subjects [REDACTED] and [REDACTED], both of whom had an excessive tortuosity in the proximal vessel segment, subjects [REDACTED] and [REDACTED], both who had target lesions located within the ostial portion of the target vessel, and subject [REDACTED] who had a documented systolic blood pressure of 183 mm Hg. Subject [REDACTED] had a reference vessel diameter of 2.5mm, outside the angiographic inclusion criterion. All of the above subjects should have been excluded based on the inclusion/exclusion criteria.

You also failed to perform all required tests at study visits. Your records contained instances where study procedures, including laboratory testing, were either not performed or were not consistently followed at scheduled examinations. For example, subjects [REDACTED], [REDACTED], and [REDACTED] did not have the total creatine kinase measurement performed as required by the study treatment procedures. Subjects [REDACTED], [REDACTED], and [REDACTED] were not evaluated with a 12-lead electrocardiogram per study treatment procedures. Subjects [REDACTED] and [REDACTED] did not have their 30-day post procedure follow-up performed within the required time frame as scheduled (3-5 weeks).

The above violations are not intended to be an all-inclusive list of deficiencies that may exist in the clinical study. We recommend that you review your records for other deficiencies and correct them accordingly. As a clinical investigator, it is your responsibility to ensure that the investigation in which you participate is conducted in accordance with applicable FDA regulations. It is important for a clinical investigator to understand that unless the physical safety of a subject demands otherwise, the treatment of study subjects must adhere to the requirements of the investigational plan.

Please acknowledge receipt of this letter within 15 working days, including supporting documentation of the specific steps you have taken or will take to correct these violations

Page 3 -- Barry S. George, M.D.

and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. In your response, provide a complete list of your open investigational studies and postmarket studies, including the name of the study sponsor, the date of IRB approval, and application number.

Failure to respond to this letter and take appropriate corrective action could result in enforcement action without further notice. In addition, FDA could begin initiation of disqualification proceedings in accordance with 21 CFR 812.119.

Please direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson, Consumer Safety Officer. If you have questions, you may contact Mr. Hopson at (301) 594-4720, extension 128. We have sent a copy of this letter to our Cincinnati District Office at 6751 Steger Drive, Cincinnati, Ohio 453267-3097. We request that you copy the district on your response.

Sincerely yours,

Michael E. Marcellini
for Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

cc: PURGED COPIES

James Lewis, M.D.
Chair, Institutional Review Board
Riverside Hospital
3535 Olentangy River Road
Columbus, Ohio 43214

