



JUN 25 2003

WARNING LETTER

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

VIA FEDERAL EXPRESS

Gerald M. Burma, M.D.
Parma Community General Hospital
6525 Powers Boulevard
Parma, Ohio 44129

Dear Dr. Burma:

The purpose of this letter is to inform you of objectionable practices and activities found during a Food and Drug Administration (FDA) inspection at your clinical site and to request a response. During the period of November 13, 2002 – January 17, 2003, Mr. Stephen J. Kilker, an investigator from FDA's Cincinnati District Office, conducted an inspection of your clinical investigation which used significant risk study devices in [REDACTED]. The purpose of the inspection was to determine whether your activities as a sponsor and principal investigator of investigational studies with significant risk devices complied with applicable FDA regulations.

The inspection focused on your study protocol at Parma Community General Hospital entitled [REDACTED]. Your protocol, which was approved by your Institutional Review Board (IRB), stated that the study was being conducted to determine whether [REDACTED] performed safely and effectively in patients considered high risk for [REDACTED]. The [REDACTED] used in this study are devices as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 321(h)].

The inspection was conducted under a program designed, in part, to ensure that data and information contained in applications for Investigational Device Exemptions (IDEs) are scientifically valid and accurate. Another objective of this program is to ensure that human subjects are protected from undue hazard or risk during the course of the scientific investigations.

Our review of the inspection report submitted by the district office revealed violations of the requirements of Section 520(g) of the Act [21 U.S.C. 360j(g)] and the regulations found at Title 21, Code of Federal Regulations (21 CFR), Part 50 – Protection of Human Subjects and Part 812 – Investigational Device Exemptions. You received a Form FDA-483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations, and Mr. Kilker discussed those observations with you and [REDACTED].

Jacqueline Potelecki. The violations and our subsequent review of the inspectional report are summarized below.

1. Failure to obtain FDA approval prior to beginning the study [Section 520(g) (21 U.S.C. 360j(g)) and 21 CFR 812.40, 812.42, 812.110(a)]

The Act and its implementing regulations set out a scheme for the study of investigational medical devices per 21 U.S.C. 360j(g) and 21 CFR Part 812. During the inspection, Mr. Kilker documented that you conducted a clinical investigation at Parma Community General Hospital involving [REDACTED] subjects, beginning on August 10, 1999, the date of IRB approval, and ending on October 8, 2002. He also documented your intent to initiate another clinical investigation, as noted in your correspondences dated September 9, 2002, and September 13, 2002, to the reviewing Institutional Review Board (IRB).

You informed Mr. Kilker that you conducted a similar [REDACTED] study at [REDACTED]. Records obtained from a separate FDA inspection at [REDACTED] confirm the existence of an IRB-approved clinical study entitled "[REDACTED]" in which you were listed as the principal investigator. The records indicated your study to be the first of three phases and that [REDACTED] subjects would be treated.

You did not obtain approval from FDA of an IDE before conducting the studies at Parma Community General Hospital and [REDACTED]. Because your studies were conducted to determine the safety and effectiveness of using [REDACTED] in a manner not cleared by FDA, you were required to have an FDA-approved IDE application before you could legally conduct such studies.

2. Failure to follow the conditions of approval imposed by the IRB and failure to report adverse events to the IRB [21 CFR 812.110(b)]

Pursuant to 21 CFR 812.110(b), an investigator shall conduct an investigation in accordance with the conditions of approval imposed by the IRB. However, you failed to perform all required tests at study visits. A review of 15 case histories revealed numerous instances where study procedures, including laboratory testing, were either not performed or were not consistently followed at scheduled examinations. For example: 1) the activated clotting time was not maintained for [REDACTED] subjects; 2) the cholesterol profile testing was not done for [REDACTED] subjects; 3) [REDACTED] subject was unable to give informed consent; 4) the diagnostic procedure was not performed for [REDACTED] subjects; 5) ultrasound was not done at six months for [REDACTED] subjects; 6) physical examination at six months was not done for [REDACTED] subjects; and 7) [REDACTED] subjects were implanted with devices smaller in size than that stated in the study protocol.

You also failed to promptly report adverse events to the IRB, as required by 21 CFR 812.150(a)(1). You did not report 14 adverse events at all, and you reported five adverse events months after their occurrence.

3. Failure to obtain adequate informed consent [21 CFR 50.25(a) and 812.100]

The basic elements required of informed consent are set forth in 21 CFR 50.25(a) and include a description of the procedures to be followed. Investigators are responsible for ensuring that informed consent is obtained in accordance with the regulations per 21 CFR 812.100.

You failed to obtain adequate informed consent. The informed consent used and signed by the subjects does not disclose all treatment and testing procedures to be followed during the course of the investigation.

4. Failure to prepare and maintain accurate, complete, and current records relating to your conduct of the investigation [21 CFR 812.140(a)(3), 812.140(a)(5), 812.150(b)(1), and 812.150(b)(6)]

The regulations require investigators to keep records and to prepare and submit reports of clinical investigations per 21 CFR 812.140 and 812.150. You did not maintain complete, accurate, and current records relating to the clinical investigation. For example, for [REDACTED] subjects, there was no supporting data, such as hospital medical records, to confirm information contained in their case histories to demonstrate their eligibility in terms of [REDACTED]

The deviations cited above are not intended to be an all-inclusive list of deficiencies at your site. As the sponsor and the clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations.

You should immediately cease conducting clinical investigations in which you implant the [REDACTED] and any other [REDACTED] in the [REDACTED] of human subjects. Conducting such clinical investigations without an approved IDE application is prohibited under Section 301(q)(1) of the Act [21 U.S.C. 331(q)(1)]. Continued study of these devices for uncleared uses without an IDE will be considered by FDA to be a knowing violation of the Act.

Before continuing research with [REDACTED] you should receive approval of an IDE application. The information to be included in an IDE application and the procedures for submitting an IDE application is set forth in 21 CFR 812, Subpart B – Application and Administrative Action.

Information to assist you in preparing your IDE application is available in the “IDE Manual.” The manual also includes information on the regulations pertaining to the protection of human subjects and to IRBs, a discussion of the IDE requirements, the responsibilities of the sponsor, and a guideline for the monitoring of clinical investigations. The manual is available on the Internet at the following address: <http://www.fda.gov/cdrh/manual/idemanul.html>. The manual may also be obtained from the Division of Small Manufacturers International and Consumer Assistance (DSMICA). They may be contacted by telephone at (800) 638-2041, by fax at (888) 361-4011, or by electronic mail at dsma@cdrh.fda.gov.

Your IDE application should be submitted, in triplicate, to:

IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

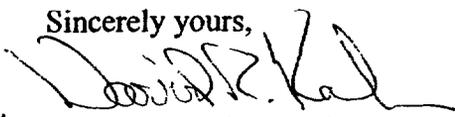
Within 15 days, you should respond to this letter in writing. You should be aware that FDA considers your actions to be violations of the law which may result in FDA taking enforcement action without further notice to you. These actions include, but are not limited to, seizing product inventory, obtaining an injunction to prevent further violations of the law, assessment of civil money penalties, and criminal prosecution.

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 I (HFZ-311), 2098 Gaither Road, Rockville, Maryland 20850. Attention: Kevin Hopson, Consumer Safety Officer.

A copy of this Warning Letter was sent to the Food and Drug Administration’s Cincinnati District, 6751 Steger Drive, Cincinnati, Ohio 45237. We request that a copy of your response also be sent to that office.

Please direct all questions concerning this matter to Mr. Hopson at (301)594-4720, ext 128.

Sincerely yours,


for
Timothy A. Ulatowski
Director
Office of Compliance
Centers for Devices and
Radiological Health