DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

M2987N

WARNING LETTER

AUG 30 1999

FEDERAL EXPRESS

Mr. Michael Porter
President
Family Medical Center IRB
209 North 16th Street
Hot Springs, South Dakota 57747

Dear Mr. Porter:

During the period of April 19 through April 21, 1999, Mr. Howard A. Burmester, an investigator with the Food and Drug Administration (FDA), Minneapolis District Office, conducted an inspection of the Institutional Review Board (IRB) at the Family Medical Center. The purpose of that inspection was to determine whether the IRB's activities and procedures relating to clinical studies of FDA-regulated products complied with applicable FDA regulations.

Our review of the inspection report and exhibits submitted by the district office revealed that there were serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 56–Institutional Review Boards, Part 50–Protection of Human Subjects, and Part 812-Investigational Device Exemptions. These deviations were listed on the Form FDA-483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. The FDA-483 was annotated to reflect your promise to take corrective action(s). The description of violations that follows is not intended to be an all-inclusive list of IRB deficiencies.

1. **Failure to prepare and maintain adequate written procedures as required by 21 CFR 56.108.**

   The policies and procedures manual that the Family Medical Center IRB has in place is inadequate in that it contains references to the authority and responsibility of the Southern Hills Hospital Advisory Board. For example, the manual requires that members "shall be appointed by the President of Southern Hills Hospital Advisory Board," and that one member from the Southern Hills Advisory Board "shall" be represented on the IRB. This is conflicting since the board disbanded on December 31, 1998, with the closing of the Southern Hills Hospital.

2. Failure to prepare and maintain adequate documentation of IRB activities as required by 21 CFR 56.115(a)(2), (5), and (6); and 812.66.

a) The IRB meeting minutes lack sufficient detail to show attendance at meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; and a written summary of the issues discussed and their resolutions. For example, minutes of the 2/25/98 meeting do not:

- identify who presented the information for the [redacted]
- describe the purpose or input provided by the consultant;
- mention the considerations made in approving the [redacted] such as whether or not the device was considered a significant or non-significant risk (which would cause the IRB to require submission of an IDE) in accordance with 21 CFR 812.66;
- sufficiently describe a vote for determination of "significance" of the device, or a vote for acceptance of the study;
- indicate if a tally of votes was made; and
- mention a vote or approval of the original "Information and Informed Consent."

In addition, the "Amendments to the IRB Minutes of Feb 25, 1998" lack:

- a date, which would serve to indicate when the amendments were added;
- an explanation for the need, decision, or vote to accept the changes recommended;
- a record of attendance;
- an explanation of "who" determined that there was no risk;
- an explanation that identifies the study or research under consideration; and
- an indication of a vote or what considerations were made in electing Mr. Porter to a position formerly held by [redacted]

The minutes of the 11/2/98 meeting are inadequate in that they do not:

- identify the IRB members that were present during this meeting– therefore, there is no documentation to show that enough members attended to represent a quorum, as required by your Policies and Procedures Manual;

- indicate whether or not [redacted] request to study significant changes to the research relating to [redacted] was being considered as a change in the original protocol; and
- provide an explanation of the changes made to the Information and Consent Form of October 15, 1998.

b) The IRB sent a letter to [redacted] requesting that he report to the IRB at the next scheduled meeting, August 11, 1998. The IRB has no records of minutes of that meeting.

c) The IRB lacks adequate documentation of IRB members. For example, the IRB does not have a list of IRB members identified by name, earned degrees, representative capacity, indications of experience and employment sufficient to describe each member's chief anticipated contributions to IRB deliberations. There is no description of affiliation with employment or membership with the board, stockholders, paid or unpaid consultants, as defined in your own Policies & Procedures.

The Policy and Procedures Manual, or equivalent record, doesn't identify the current members of the board, with a Curriculum Vitae or other description, to show how they contribute to the diversity required by regulation and the IRB's Policy and Procedures.

In the 2/25/98, meeting minutes, [redacted] is identified as a consultant. The IRB lacks documentation to show acceptance of [redacted] as a consultant and his functional responsibility.

d) The IRB lacks documentation to verify that someone from the IRB, with the knowledge and experience of medical devices similar to the one to be used in [redacted], made an in-depth review of the investigational proposal; or that the IRB received consultation from someone in this capacity to make a final approval.

e) The IRB lacks records of training of new IRB members or documents to show they, and existing members, are familiar with the policies and procedures the IRB has established.

f) The IRB lacks documentation to show that IRB members received study information before IRB meetings. The IRB Policy and Procedures Manual states that "review information will be forwarded to the Chairperson two weeks prior to the meeting." Without receiving the information, the IRB cannot make a review of the study as required by 21 CFR 56.109.

g) The records kept for [redacted] study contain three different consent forms. Two consent forms are kept in the packet of original information provided to each IRB member and the third is included in the bound information manual provided as the latest information given to the subjects of the study. The IRB's minutes of the various meetings only describe the submission and approval of one Amended Revision of the Consent Form; there is no record of the approval of the original Consent Form to show when the study was approved.

An institution, or where appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities.

3. Failure to require that subjects receive an adequate informed consent as required by 21 CFR 56.109.

The IRB failed to require that the informed consent include a complete explanation of the research in accordance with 21 CFR 50.25. For example, the following required items are missing from the consent:

Risks/Benefits – Information provided to subjects in the [redacted] was approved by the IRB in a meeting on 7/21/98. The IRB has no evidence that the review of the protocol included the risk, benefit, or reason for the use of a combination of vitamins, minerals, and nutritional supplements in conjunction with electrical stimulation.

We acknowledge receipt of a copy of the May 24, 1999, letter, addressed to our Minneapolis District Office in response to the Form FDA-483. This letter will be made a part of our official files. Your letter reflects an understanding of the observations FDA noted. You explained the IRB's ongoing efforts to bring the institution into compliance. In addition, you indicate that the IRB is adopting the standard operating procedures of the Black Hills Care Network. If these procedures have been revised and implemented, we request that you submit a copy to us as part of your response to this letter. To assist you, we have enclosed a copy of the FDA Information Sheets, Guidance for Institutional Review Boards and Clinical Investigators. This is a valuable resource for writing standard operating procedures.

Please advise this office, in writing, within fifteen 15 working days of receipt of this letter, of the additional specific steps you have taken to correct these violations and to prevent recurrence of similar violations in current or future studies. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your failure to respond may result in further regulatory action without notice, including disqualification of the IRB.

Your response to this letter should be directed 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: Pamela M. Reynolds. A copy of this Warning Letter has been sent to the FDA's Minneapolis District Office, 240 Hennepin Avenue, Minneapolis 55401. We request that a copy of your response also be sent to that office and to the Office for Protection from Research Risks (OPRR).

Sincerely yours,

Charmaine Korner, RPh

for

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

Enclosure: FDA Information Sheets

cc: Michael Carome, M.D.
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