



Union Memorial Hospital

Experience Matters

Vascular Services

Non Invasive Testing
Diagnostic Angiography
Percutaneous Intervention
Vascular Surgery

DEC 8 2003

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Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch (HFZ-312)
2094 Gaither Road
Rockville, Maryland 20850

Attention: Rachael Solomon

December 3, 2003

Dear Ms. Solomon,

Attached please find an electronic copy of our response to the warning letter issued June 19, 2003 to Dr. Frank J. Criado. We are requesting that the response be posted on the web site with the warning letter in accordance with the guidelines of the pilot program.

Thank you for your attention to this matter.

Sincerely,



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July 7, 2003

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch (HFZ-312)
2094 Gaither Road
Rockville, Maryland 20850
Attention: Rachael Solomon

Dear Ms. Solomon,

Below please find additional responses related to issues brought up in the warning letter issued June 19, 2003.

“Failure to report unanticipated adverse device effects or deaths in a timely manner to the reviewing IRB. [21 CFR 812.159(a)(1)].”

- The six adverse events related to only two patients; as Principal Investigator, it was my understanding – at the time of their occurrence - that the adverse events had been reported in a timely fashion. Unfortunately, we have been unable to find documentation of such reports and, therefore, all such events have been (again) reported to the IRB.
- Effective immediately, a copy of the stamped receipt (from the IRB) of all reported adverse events will be kept on file in our research office.
- The research staff has received extensive training in IRB policies and procedures as well as FDA regulations. Sources of information have included the FDA auditor, IRB representatives, as well as staff attendance of a recent FDA-sponsored symposium by the Society of Clinical Research Associates.

“Failure to obtain IRB approval before allowing any subjects to participate. [21 CFR 812.110(a)].”

- IRB approval for the low risk study was allowed to lapse March 25, 2000. Unfortunately and regrettably, I only learned of this oversight after five additional study patients had been enrolled and received stent-graft implants. I notified the IRB immediately upon learning of such mishap, and undertook to reinstate the study in the most expeditious and proper manner. I would like to reiterate once again that neither patient safety nor the integrity of the clinical study were compromised in any way by such lapse. Clinical outcomes were all successful, and data collection and documentation proceeded in normal fashion.
- The Clinical Research Coordinator responsible for the oversight was terminated.
- A database has been implemented to indicate study/consent renewal dates, as well as a computer generated reminder of all expiration dates.
- The IRB is now printing expiration dates on the stamped approved consent for each study.
- In regards to the high risk study, I would like to reiterate what was stated in my response letter (to form 483) dated 3/18/03: “Two studies were submitted at the same time for IRB approval; [REDACTED] High Risk and [REDACTED] Low Risk. Approval was granted for both studies; the IRB approval letters, dated March 25, 1999 were identical. The titles for both studies were identified on the IRB approval; however, both titles were same, without indication of High Risk versus Low Risk. This has caused a great deal of confusion. In the end, the outcome of our investigation is that the [REDACTED] High Risk study was approved on March 25, 1999. Therefore, the five subjects in question ([REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED]) were implanted after proper IRB approval indeed.” Additionally, the IRB has implemented a new procedure whereby each study is assigned a separate identifier number.

“Failure to conduct the study in accordance with the investigational plan. [21 CFR 812.100 and 812.110 (b)].”

- The staff and investigator have strived to learn more about and received additional training regarding regulatory requirements and responsibilities, as well as good clinical practices. This has come by way of IDE industrial sponsors, the FDA auditor, as well as attendance to the FDA-sponsored symposium/workshop referred to above.
- A schedule of events for each clinical study has been posted in the research office for quick reference to assure familiarity and compliance with protocol requirements and timelines.

I hope the above responses represent a clear portrayal of actions taken and of the new policies that have been implemented to comply with regulations and prevent such occurrences in the future. We remain committed to patient safety and to the highest standards of clinical research.

Sincerely,

Frank J. Criado, MD
Director, Center for Vascular Intervention
Chief, Division of Vascular Surgery