

the investigational plan and failure to obtain such approval from the reviewing IRB and FDA, where the changes or deviations could have affected the rights, safety, or welfare of human subjects. [21 CFR 812.150(a)(4), 21 CFR 812.100, and 21 CFR 812.110(b)]

As an investigator, you are responsible for ensuring the investigation is conducted in accordance with the signed investigator agreement, the investigational plan, and applicable FDA regulations. In addition, you are responsible for notifying the sponsor and the reviewing IRB of any deviations from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan and where, as here, changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and the IRB.

You enrolled subjects that met exclusion criteria without sponsor, IRB and FDA approval of these protocol deviations. Examples of these failures include, but are not limited to, the following:

A) Exclusion Criteria E. states, (b)(4)
(b)(4)
(b)(4)

Subject Number	
(b)(4)	(b)(4)

B) Exclusion Criteria P. states, (b)(4) ”
(b)(4)

Subject Number	
(b)(4)	(b)(4)

Please provide copies of policies and procedures, with expected completion dates, that are being developed and implemented to ensure both eligibility of subjects and documentation of that eligibility. In addition, please provide copies of policies and procedures for ensuring appropriate approvals of protocol deviations are obtained in accordance with the protocol, the reviewing IRBs policy and Federal Regulations.

Failure to prepare and submit complete, accurate, and timely reports of unanticipated adverse device effects. [21 CFR 812.150(a)(1)]

As an investigator, you are responsible for ensuring complete, accurate, and timely reports of any unanticipated adverse device effects occurring during an investigation are submitted to the reviewing IRB and sponsor as soon as possible, but in no event later than 10 working days after you first learn of the effect. You failed to report unanticipated adverse device effects in accordance with this regulation. Examples of your failure include, but are not limited to, the following:

Subject number	Date of	Event	Date event occurred	Date reported to IRB	Date reported to sponsor
(b)(6)	(b)(4)	(b)(4)		(b)(6)	

Please provide copies of policies and procedures, with expected completion dates that are being developed and implemented to ensure documentation and reporting of unanticipated adverse events performed in accordance with the protocol, the reviewing IRB requirements, and applicable Federal Regulations.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations.

The regulations in 21 C.F.R. Part 812 describe sponsor responsibilities as well as those of investigators. IRB responsibilities are spelled out in 21 C.F.R. Part 56, Institutional Review Boards. These three sets of responsibilities overlap to ensure appropriate conduct of clinical studies and the protection of the rights and welfare of participating subjects. Therefore, though the sponsor and IRB involved in your study may have been remiss in fulfilling their responsibilities, you are still held responsible for knowing and following the regulations pertinent to your activities as a clinical investigator in FDA-regulated studies.

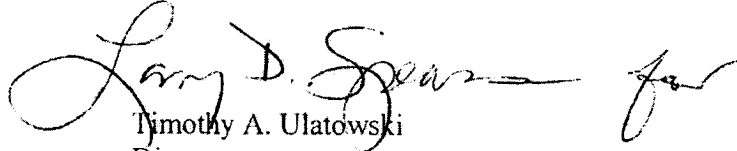
Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 C.F.R. 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the [FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators](http://www.fda.gov/oc/ohrt/irbs/), which can be found at <http://www.fda.gov/oc/ohrt/irbs/>. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to: Attention: Doreen Kezer, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to Los Angeles District Office at 19701 Fairchild, Irvine CA, 92612. Please send a copy of your response to that office.

If you have any questions, please contact Doreen Kezer, (240) 276-0125, e-mail
Doreen.kezer@fda.hhs.gov.

Sincerely yours,



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

cc. (purged)

(b)(4)

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