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Food and Drug Administration  
Center for Devices and  
Radiological Health  
2098 Gaither Road  
Rockville, MD 20850**Via Federal Express**  
**WARNING LETTER**

Willard M. Kniep, Ph.D.  
Vice President of Academic Affairs  
Pacific University  
2043 College Way  
Forest Grove, Oregon 97116

Dear Dr. Kniep:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB), to discuss the written response to the deviations noted, and to request your prompt response to the remaining issues. The inspection took place during the period of September 3 through 5, 2002, and was conducted by Mr. Robert D. Tollefsen, Mr. Carl A. Anderson, and Mr. Michael J. Lackey, investigators from FDA's Seattle District Office. The purpose of the inspection was to determine whether IRB procedures complied with Title 21, Code of Federal Regulations (21 CFR), Part 50- Protection of Human Subjects, Part 56 – Institutional Review Boards, and Part 812 – Investigational Device Exemptions. These regulations apply to clinical studies of products regulated by the FDA.

Our review of the inspection report submitted by the district office revealed serious violations from pertinent regulations. You received a Form FDA 483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed. We acknowledge receipt of a September 27, 2002, letter from Karl Citek, O.D., Ph.D., FAAO, the IRB Chair, that includes a list of action items to be discussed at the October 10 meeting of the IRB in response to items listed on the Form FDA 483. Deviations noted include:

**Failure to prepare and follow written standard operating procedures (SOPs) governing the functions and operations of the IRB (21 CFR 56.108 and 21 CFR 56.115(6)).**

Inspectional review revealed a lack of written procedures governing the day-to-day operations of the IRB. The only document available at the time of the inspection, "Institutional Review Board Pacific University, Use of Human Subjects: IRB Guidelines," was a handout prepared by [REDACTED] for use in a university course. There is no indication that this document was prepared for use by the IRB. Moreover, the document only describes general functions of an IRB. According to 21 CFR 56.108(a)

and (b), an IRB is required to have and follow written procedures for its operations and functions.

**Failure to review proposed research at convened meetings of the IRB (21 CFR 56.108(c)).**

As described by Dr. Citek during the inspection and summarized in a memorandum from an informational meeting of the IRB dated April 5, 2000, research proposals receive an in-depth review by the IRB Chair who then prepares research study packets to be disseminated to all IRB members, along with IRB review forms. Once members complete their review, they return their comments, as well as their vote for approval or disapproval, to the Chair via a completed review form, an e-mail message, or in a phone conversation. Except when an expedited review procedure is used, as described in 21 CFR 56.110, an IRB is required to review proposed research at a convened meeting at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas.

**Failure to provide adequate continuing review of approved studies (21 CFR 56.109(f)).**

Inspectional findings indicate that Dr. Citek reviews progress and final reports on receipt and then places the reports in the study file. These reports are not distributed to other IRB members. Federal regulation (21 CFR 56.109(f)) requires an IRB to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. Also, 21 CFR 56.111 describes the criteria for review, which must occur at convened meetings, unless expedited review is appropriate as described in 21 CFR 56.110.

**Failure to maintain records of IRB deliberations (21 CFR 56.115(a)(2)).**

FDA regulations require IRB activities to be adequately documented. The minutes of IRB meetings must be in sufficient detail to show the attendance at the meetings, actions taken, the specifics of who voted and how, the basis for requiring changes in or disapproving research, and a written summary of the discussion of controverted issues and their resolution. Your IRB did not have minutes documenting IRB meetings convened for the purposes of review of research because, as stated above, your IRB failed to review and approve research at convened meetings as required. Your IRB also did not provide any other records showing the deliberations by IRB members on research that has been approved by your IRB.

**Failure to notify investigators in writing of decisions regarding approval of research (21 CFR 56.109(e)).**

Records reviewed for the [REDACTED] and [REDACTED] studies revealed no record of correspondence with the investigators in these studies regarding approval

of the study. An IRB is required to notify investigators in writing of its decision to approve or disapprove the proposed research activity or of modifications required to secure IRB approval.

In addition, there was no record of any correspondence with the individual investigators at any time. IRBs are required by 21 CFR 56.115(a)(4) to maintain copies of all correspondence between the IRB and the investigators.

The deviations listed above are not intended to be an all-inclusive list of the deficiencies noted. The IRB is responsible for adhering to each applicable requirement of the law.

Dr. Citek's response states that the IRB was to consider, at a convened meeting on October 10, 2002, an agenda of items to correct the deviations noted. The agenda was to include discussion of the requirements for IRB membership and the make-up of the board; the need to discuss business at convened meetings; and the need to write and follow written procedures for the day-to-day operations of the IRB.

Within fifteen (15) working days of receipt of this letter, please inform FDA of the results of the October 10 meeting, including a copy of the meeting minutes. Please also include a copy of the written SOPs that have been drafted to describe the functions and operations of the IRB or provide a time table for submitting this document if it is not yet complete.

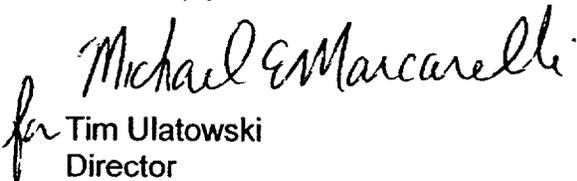
Please send your response, including all of the information requested above, to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Jean Toth-Allen, Ph.D. Failure to respond or to take appropriate corrective actions can lead to additional administrative or regulatory actions without further notice, including, as described in 21 CFR 56.120 and 56.121, withholding approval of new studies, directing that no new subjects be added to on-going studies, terminating on-going studies, notifying relevant State and Federal regulatory agencies, and disqualification of the IRB.

A copy of this letter has been sent to FDA's Seattle District Office, 22201 23<sup>rd</sup> Drive, SE, Bothell, Washington 98021. We request that a copy of your response also be sent to that office.

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If you have any questions, feel free to contact Dr. Toth-Allen at (301) 594-4723, extension 141.

Sincerely yours,

  
for Tim Ulatowski  
Director  
Office of Compliance  
Center for Devices and Radiological  
Health

cc:

Karl Citek, O.D., Ph.D., FAAO  
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