



NOV 15 2006

## WARNING LETTER

VIA FEDERAL EXPRESS

Aqueous Biomedical, Inc.  
Michael J. Wilcox, Ph.D.  
6555 Delmonico Drive  
Apt. 212  
Colorado Springs, CO 80919

Dear Dr. Wilcox:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Aqueous Biomedical, Inc., from August 7 through August 10, 2006, by an investigator from the FDA Denver District Office. The purpose of this inspection was to determine whether activities as sponsor of the clinical study titled [REDACTED] [REDACTED] complied with applicable federal regulations. The [REDACTED] is a device 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). This letter also requests prompt corrective action to address the violations cited.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed several violations of Title 21, Code of Federal Regulations (21 C.F.R.) Part 812 -- Investigational Device Exemptions. At the close of the inspection, the FDA investigator presented an inspectional observations form FDA 483 for your review and discussed the observations listed on the form with you. You did not submit a response to the form FDA 483 consequently, only the deviations noted on the FDA 483 are discussed below:

**1. Failure to accurately document device shipment records [21 CFR 812.140(b)(2)].**

Pursuant to 21 CFR 812.140(b)(2), a sponsor shall maintain accurate, complete and current records relating to shipment and disposition of the device. Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition

shall describe the batch number or code marks of any device returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

You failed to maintain accurate device accountability records that include the name and address of the consignees receiving the devices, type and quantity of devices, date of shipments, and batch/serial numbers. Examples of this failure include but are not limited to the following:

- a. During the inspection, you provided FedEx receipts, pages from your personal calendar, and e-mails pertaining to device shipments, however, they are not considered accurate device accountability records that include the name and address of the consignees receiving the devices, type and quantity of devices, date of shipments, and batch/serial numbers.
- b. During the inspection you presented a [REDACTED] with the serial number [REDACTED] and the lot number [REDACTED]. A case report form for subject [REDACTED] includes the identical serial number ([REDACTED]) and lot number [REDACTED].
- c. You informed the FDA investigator that [REDACTED] devices were shipped to clinical investigators. However, when they became obsolete you failed to maintain documentation of the disposition of all the obsolete devices.

**2. Failure to maintain accurate, complete, and current records relating to an investigation [21 CFR 812.140(b)(6)].**

As per regulation, a sponsor shall maintain any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation. You failed to adhere to the above stated regulation; examples of this failure include but are not limited to the following:

- a. You failed to obtain copies of IRB approved protocols from [REDACTED] and the [REDACTED] Review Board.
- b. You failed to obtain copies of the investigator site visit reports for [REDACTED] ([REDACTED]) and [REDACTED] ([REDACTED]).
- c. You failed to obtain copies of the annual reports from [REDACTED] ([REDACTED]).

**3. Failure to submit reports to reviewing institutional review boards [21 CFR 812.150(b)(5)].**

Under 21 CFR 150(b)(5), sponsors are responsible to submit a progress report to all reviewing IRB's at regular intervals, and at least yearly.

You failed to submit progress reports as required by regulation to [REDACTED], who oversees the research for the [REDACTED].

**4. Failure to obtain an adequate signed investigator agreement for each participating investigator [21 CFR 812.43(c)(5)].**

Pursuant to 21 CFR 812.43(c), a sponsor is required to obtain from each participating investigator a signed agreement that shall include sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement to FDA. The agreement also must contain a commitment from the investigator to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study.

You failed to obtain a signed investigator agreement from [REDACTED] and [REDACTED] that includes financial disclosure information.

**5. Failure to possess written monitoring procedures and failure to ensure proper monitoring of the investigation [21 CFR 812.25(e) and 21 CFR 812.40].**

Pursuant to 21 CFR 812.25, an investigational plan shall include written procedures for monitoring the investigation and the name and address of any monitor. Under 21 CFR 812.40, a sponsor is responsible for ensuring proper monitoring of the investigation.

You failed to provide written monitoring procedures for monitoring the study. The [REDACTED] does not include monitoring procedures (i.e. monitoring schedule, adherence to protocol, verification of source documents to case report forms) for monitoring the study. In addition, you were not able to provide monitoring correspondence or reports therefore you failed to ensure proper monitoring of the investigation.

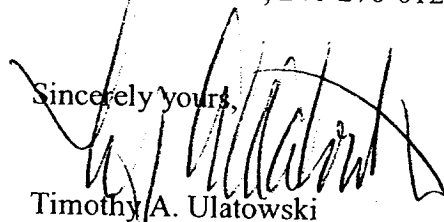
The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a study sponsor to ensure compliance with the Act and applicable regulations.

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 study sponsor. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. 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 the Denver District Office, 6<sup>th</sup> & Kipling Street (P.O. Box 25087), Denver, CO 80225-0087. Please send a copy of your response to that office.

If you have any questions, please contact Doreen Kezer, 240-276-0125, Doreen.Kezer@fda.hhs.gov.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Timothy A. Ulatowski', written over the 'Sincerely yours,' text.

Timothy A. Ulatowski

Director

Office of Compliance

Center for Devices and Radiological Health