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Inspections, Compliance, Enforcement, and Criminal Investigations

Otologics LLC 3/5/10



Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

MAR 5 2010

WARNING LETTER

VIA FEDERAL EXPRESS

Jose H. Bedoya
President and CEO
Otologics LLC
5445 Airport Boulevard
Boulder, CO 80301-2308

Dear Mr. Bedoya:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Otologics LLC from October 26, through November 19, 2009 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 **(b)(4)**, complied with applicable federal regulations. The 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 and discusses your December 8, 2009 written response to the noted violations.

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 CFR), Part 812--Investigational Device Exemptions, and Section 520(g) (21 U.S.C. 360j(g)) of the Act 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. The deviations noted on the Form FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

1. Failure to maintain accurate, complete, and current records of correspondence relating to an investigation [21 CFR 812.140(b)(1)].

Sponsors are responsible for maintaining accurate, complete, and current records of all correspondence with the FDA. Examples of your failure include, but are not limited to, the following:

- The protocol deviation section of Supplement 61, dated 7/29/09 submitted to the Agency states the following: "There have been no deviations from the investigational plan..." However, there were at least 13 deviation forms found in subjects' files at site 0011, and one deviation form each at sites 0038, 0039, 0026, 0020, and 0034.
- Table 3 of Supplement 61, (b)(4) does not accurately reflect data recorded on the case report forms (CRF) for two subjects at site 0011. The CRF for subject (b)(6) and the CRF for subject (b)(6) document that (b)(4) testing was not performed on the (b)(4). Although memos (both dated 5/27/09), in each subject's file, explain testing was not performed on the (b)(4) because it is assumed (b)(4), Table 3 represents these test values as being from the **(b)(4)** for both subjects.

Your written response dated December 8, 2009 states the following in response to the unreported protocol deviations documented:

- you have a new SOP entitled **(b)(4)** to address protocol **(b)(4)** processing, of which you have already trained Otologics clinical staff;
- you will train principal investigators at all sites on this SOP;
- you will engage an independent third party to audit study data by the end of March 2010;
- the **(b)(4)** testing was not conducted for subjects at site 0011 because the site assumed **(b)(4)** in which the database will be corrected to show this as "missing data," which will also be included in the December 23, 2009 annual report to FDA;
- you will notify the site that all testing in the investigational plan must be conducted; and
- you will train site monitors to review for adherence to protocol.

Your written response regarding unreported protocol **(b)(4)** is inadequate in that you did not provide any corrective action to prevent recurrence. You provided Attachment C as documentation of training; however, it does not document training on the SOP entitled **(b)(4)**, " Please provide a copy of this SOP as well as documentation of training of the Otologics clinical staff and principal investigators at all sites. In addition, your response regarding **(b)(4)** testing that was not conducted is also inadequate in that it does not describe how you will ensure the site adheres to the protocol or how you will ensure that data on CRFs are accurate and that errors are promptly discovered and appropriately corrected. Please provide records of the site monitoring training, which should include how adherence to the protocol will be monitored as well as a copy of the December 23, 2009 report, as it has not been received in FDA as of the date of this letter.

2. Failure to maintain accurate, complete, and current device shipment records [21 CFR 812.140(b)(2)]

Sponsors are responsible for maintaining accurate, complete, and current records relating to shipment and disposition of devices. Examples of your failure include, but are not limited to, the following:

- There were at least three discrepancies at Site 0038, in that lot numbers for Single Use Kits on the invoices do not correspond with the lot numbers on the surgical report forms for subjects **(b)(6)** and **(b)(6)** as shown in the table below.

Subject	Lot # on Invoice	Lot # on Surgical Report
(b)(6)	(b)(4)	(b)(4)

(b)(6) **(b)(4)** **(b)(4)**

• At the same site, there are discrepancies in the serial numbers (SN) for the **(b)(4)** and the **(b)(4)** for subjects **(b)(6)** and **(b)(6)** as shown in the tables below. In addition, the invoice for subject **(b)(4)** and the shipping document for subject **(b)(6)** were missing for **(b)(4)** and **(b)(4)**.

Subject	(b)(4) on Invoice	(b)(4) on Shipping Document	(b)(4) on Surgical Report
(b)(6)	(b)(6)	(b)(6)	(b)(6)
(b)(6)	(b)(6)	(b)(6)	(b)(6)

Subject	(b)(4) on Invoice	(b)(4) on Shipping Document	(b)(4) on Surgical Report
(b)(6)	(b)(6)	(b)(6)	(b)(6)
(b)(6)	(b)(6)	(b)(6)	(b)(6)

Your written response states that you have updated several procedures to address investigational device accountability, specifically, the "Clinical Study Material Accountability Procedure" and the "Returned Goods Procedure." In addition, you stated that all clinical trial staff and materials management were trained to the procedures by Quality Assurance on December 1, 2009.

Your response is incomplete in that the updated procedures solely covers the shipment of and return of product but not the discrepancies noted with the records such as incorrect SNs. Please provide your corrective action to ensure accurate tracking of investigational device components, especially with regard to the lot numbers and SNs of each component used for each subject. Please provide documentation that all appropriate personnel at each site is trained on all revised procedures.

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 additional 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.

Your December 8, 2009 response to the Form FDA 483 requested a meeting with the FDA. We appreciate your willingness to address the Form FDA 483 in person. We can reconsider your request if you believe a meeting to discuss the necessary corrective actions will assist you in establishing and implementing effective corrections. 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: Anne Hawthorn, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 10903 New Hampshire Avenue, W066-3504, Silver Spring, Maryland, 20993-0002.

A copy of this letter has been sent to the Denver District Office, 6th & Kipling Street, P.O. Box 25087, Denver, CO, 80225-0087. Please send a copy of your response to that office.

The Division of Bioresearch Monitoring has developed introductory training modules in FDA regulated device clinical research practices, which are available on the FDA website. The modules are for persons involved in FDA regulated device clinical research activities. These modules are located at the following website address: <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>

If you have any questions please contact Anne Hawthorn at (301) 796-6561 or via email at anne.hawthorn@fda.hhs.gov.

Sincerely yours,

/S/

Michael Marcarelli Pharm.D. MS
Director
Division of Bioresearch Monitoring
Office of Compliance
Center for Devices and
Radiological Health

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