



MAR 21 2007

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

WARNING LETTER

VIA FEDERAL EXPRESS

Briant E. Benson
CEO/President
Bentec Medical, Inc.
1380 E. Beamer Street
Woodland, CA 95776-6003

Dear Mr. Benson:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Bentec Medical, Inc., from October 23 to November 2, 2006 by an investigator from the FDA San Francisco District Office. The purpose of this inspection was to determine whether your activities as sponsor of the clinical study

IDE _____, 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 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 applications (PMA), 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 serious violations of Title 21, Code of Federal Regulations (21 CFR) 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. 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 ensure proper monitoring of the investigation, to ensure IRB review and approval, and to submit an IDE application to FDA, and receive FDA approval of the IDE before beginning the investigation [21 CFR 812.40 and CFR 812.42].**

Pursuant to 21 CFR 812.40 and 812.42, sponsors are responsible for ensuring proper monitoring of the investigation, ensuring that IRB review and approval are obtained, and for submitting an IDE application to FDA and obtaining approval before beginning an investigation. Examples of your failure to adhere to these regulations include, but are not limited to, the following:

A. You failed to ensure that approval from FDA was obtained before shipping the _____ device to any investigator. You first received a conditional approval of your IDE from FDA on _____. However, you made the following shipments of the investigational product prior to receiving approval from the FDA:

1. From _____ until _____ you shipped at least _____ devices to clinical investigator _____
2. You shipped _____ device to _____ on _____ and another device on _____
3. You shipped at least _____ devices to _____ on _____ and _____

Your response states that in order to avoid this issue in the future, such devices will be in quarantine control, and only released by Quality Assurance. Your response also states that product release shall be only for legitimate sales for export or to qualified investigators participating in a _____ clinical investigation under Agency approval of an IND application. Please note that IND applications pertain to drug studies. Because the _____ is a device, the appropriate application is an IDE. Your response is inadequate, in that it does not indicate how such devices will be controlled prior to distribution. Please provide standard operating procedures (SOPs) that detail the storage, distribution, and release of investigational products.

B. You failed to ensure that IRB review and approval was obtained before making the above shipments. There was no record of IRB review and approval of a study protocol or informed consent form (ICF) available at your site during the FDA inspection. (Under 21 CFR 812.140(b)(1), all correspondence with any investigator and with any IRB must be maintained.) FDA's separate inspection of _____ indicates that _____ received a conditional approval of this study protocol from an IRB at _____ site for the _____ time in _____

Your response is inadequate in that it does not address this issue. Please provide the corrective and preventive actions you have taken or plan to take to ensure that IRB approval of investigational protocols and ICFs is obtained prior to the shipment of investigational devices.

C. You failed to monitor the use of the distributed devices. During the inspection, you indicated that there has been no monitoring of the clinical trial. Furthermore, FDA's separate inspection of _____ a clinical investigator in your study, revealed multiple serious violations of FDA investigational device regulations, which you would have discovered and have been obligated to take action to stop and correct, in accordance with 21 CFR 812.46, if you had ensured proper monitoring.

Your response is inadequate in that it does not address the issue. Please provide additional information regarding corrective and preventive actions you have taken or plan to take, including the development of any SOPs, training, etc.

2. Failure to ensure that investigational devices are only shipped to qualified investigators participating in the investigation [21 CFR 812.43(b)].

Pursuant to 21 CFR 812.43(b), sponsors are responsible for ensuring that investigational devices are only shipped to qualified investigators participating in the investigation. Examples of your failure to adhere to the above stated regulation include, but are not limited to, the following:

You shipped investigational devices to the following people even though they are not included as investigators in the list of clinicians submitted in _____ as part of your IDE (as required by 21 CFR 812.20(b)(4):

- A. You shipped _____ devices to _____ on _____ and _____
- B. You shipped _____ devices to _____
- C. You shipped _____ devices to _____ and _____

Your response states that the shipments made were marketing samples provided to physicians for purposes of inputs on the design. Your response also states that in order to avoid this issue in the future, all such devices will be in quarantine control and only released by Quality Assurance, and that release shall be only for the legitimate sales as Export Only or to qualified investigators participating in a _____ clinical investigation under Agency approval of an IND application. Please note this device is subject to an IDE application, not an IND application as stated in your response. Your response is inadequate. As mentioned above, please provide any additional information regarding corrective and preventive actions you have taken or plan to take, including the development of any SOPs, training, etc.

3. Failure to obtain a signed agreement from each participating investigator [21 CFR 812.43(c)].

Pursuant to 21 CFR 812.43(c), sponsors are responsible for obtaining a signed agreement from each participating investigator. Examples of your failure to adhere to the above stated regulation include, but are not limited to, the following:

You did not obtain signed investigator agreements from the following persons participating in this study:

A. Clinical investigator _____ has not signed an investigator agreement, although at least _____ devices were shipped to _____ prior to FDA approval of the IDE and at least _____ devices were shipped to _____ after the FDA approval of the study.

B. You do not have signed investigator agreements from _____ however, you shipped _____ devices to these individuals.

Your response states that you are in the process of obtaining signed investigator agreements for the principle investigator and physicians _____ Your response does not refer to obtaining a signed investigator agreement from _____ Please be aware that investigational devices can only be shipped to the clinical investigators listed in the protocol. Neither _____ is listed as an investigator in the protocol. Your response is inadequate, in that you do not provide what steps you have taken to prevent this deviation in the future. Please provide any additional information regarding corrective and preventive actions you have taken or plan to take, including the development of any standard operative procedures (SOPs), training, etc.

4. Failure to conduct an evaluation of any unanticipated adverse effect [21 CFR 812.46(b)(1)].

Pursuant to 21 CFR 812.46(b)(1), sponsors are responsible for conducting an evaluation of any unanticipated adverse effect. Examples of your failure to adhere to the above stated regulation include, but are not limited to, the following:

Page 5 of document _____ Revision A, entitled _____ with _____ is the only document available which describes complications and adverse device effects; however, the document lacks subject identification information, dates, and other pertinent information. Two of these events are considered serious adverse effects: small bowel obstruction and deep vein thrombosis.

Your response states, in part, that you have mechanisms in place that will help to ensure the evaluation of unanticipated adverse device effects. Your response is inadequate in that it does not provide any additional information regarding how this will be achieved. Please provide the corrective and preventive actions you have taken or plan to take regarding this deficiency.

5. Failure to maintain accurate, complete, and current records of shipment and disposition of investigational devices, including the name and address of the consignee type and quantity of the device, date of shipment, and batch number or code mark, and, records of batch number or code marks of any devices 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 [21 CFR 812.140(b)(2)].

Pursuant to 21 CFR 812.140(b)(2), sponsors are responsible for maintaining accurate, complete, and current records of shipment of investigational devices, including the name and address of the consignee, type and quantity of the device, date of shipment, and batch number or code mark. They are also required to maintain records of disposition that describe the batch number or code marks of any devices 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. Examples of your failure to adhere to the above stated regulation include, but are not limited to, the following:

The shipping database did not reflect all shipments. According to the affidavit signed by _____ devices were either shipped or hand-delivered to the clinical investigator on _____ occasions. There are no records regarding the shipment of:

- A. _____ devices shipped to _____ sometime after _____
- B. _____ devices shipped to _____ sometime on or about _____
- C. _____ devices were hand-delivered to _____ sometime after _____

Your response is inadequate. It states only that a retrospective disposition status has been defined to the best of your abilities by the affidavit signed by Bentec at Woodland, CA on November 2, 2006. Please verify that you mean to refer to the affidavit signed by _____ and provided to the FDA investigator on FDA Form 463a at the time of the inspection. In addition, please explain what corrective and preventive actions you have taken to address this issue and prevent its recurrence in the future.

6. Failure to label the device as investigational [21 CFR 812.5(a)].

Pursuant to 21 CFR 812.5(a), an investigational device or its immediate package shall bear a label with the following information: the name and place of the manufacturer, packer, or distributor, the quantity of the contents, and the following statement "CAUTION-Investigational device, Limited by Federal (or United States) law to investigational use." The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

The investigational devices, _____ did not contain the proper labeling. You failed to include the statement "CAUTION-Investigational device, Limited by Federal (or United States) law to investigational use" on all domestic shipments of the investigational devices. Examples of information not included are:

- A. You shipped _____ of lot _____ and _____ of lot _____ manufactured on _____ respectively. These devices were called _____ at the time of manufacture. These products were labeled without the required caution statement.
- B. You shipped _____ of lot _____ and _____ of lot _____ to _____ These devices were labeled without the required caution statement.
- C. You manufactured and labeled at least _____ lots of the _____ without the required caution statement.

This violation was not listed on the Form FDA 483, although the FDA investigator discussed the requirements for labeling investigational devices with you, and referred you to 21 CFR 812.5 for guidance. Please provide the corrective and preventive actions you have taken or plan to take regarding this deficiency.

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.

In addition to the violations cited above, we draw your attention to 21 CFR 812.43(d), which requires sponsor to select monitors qualified by training and experience to monitor the investigation study in accordance with FDA regulations.

_____ a clinical research associate, was identified as the monitoring personnel. However, during the inspection, there was no information available regarding her qualifications, training, or experience in monitoring clinical studies.

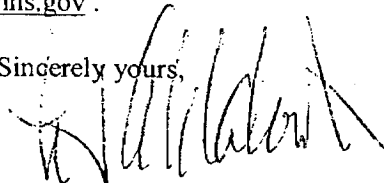
Your response states, in part, that you have mechanisms in place that will help to ensure proper monitored by qualified personnel. Your response does not address either what specific qualifications are or what your general criteria for selecting monitoring personnel are, including what training and experience is required in order for an individual to be considered qualified. In your response, please explain what actions you take to satisfy the requirements of 21 CFR 812.43(d).

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 the violations cited above 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 San Francisco District Office, 1431 Harbor Bay Parkway, Alameda, CA 94502-7070. Please send a copy of your response to that office. If you have any questions, please contact Doreen Kezer at telephone number (240) 276-0125 or at e-mail address doreen.kezer@fda.hhs.gov.

Sincerely yours,



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