



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

SEP 5 2003

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

WARNING LETTER
Via FedEx

Mr. Robert J. Jones
President and CEO
Cavitat Medical Technologies, Inc.
10691 East Bethany Drive, Suite 900
Aurora, CO 80014

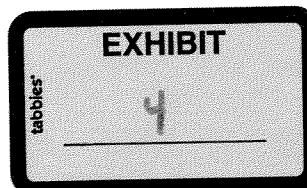
Dear Mr. Jones:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your facility and request a prompt reply. The inspection took place during the period of April 14 through April 17, 2003, and was conducted by Ms. Lori A. Medina, an investigator from FDA's Denver District. During the inspection, Robert Y. Jones, Vice President of Engineering and Production, stated that he had the knowledge and authority to provide FDA with the requested information in your absence.

The purpose of the inspection was to determine whether your activities as a sponsor/monitor of the Cavitat Ultrasonograph studies entitled "Through-Transmission Sonography (TTS) - New Technology for Detection at Low Bone Density of the Jaws: Comparison with Radiology for 92 Osteoporotic Alveolar Sites with Histopathologic Confirmation" and "Through-Transmission Sonography (TTS) - New Technology for the Evaluation of Jawbone Density and Desiccation: Correlation with Histopathology of 285 Scanned Alveolar Sites" complied with applicable FDA regulations. The Cavitat Ultrasonograph 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)).

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 (510(k)) submissions 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 submitted by the district office revealed serious violations of requirements of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions and Part 50 - Protection of Human Subjects. At the conclusion of the inspection, Robert Y. Jones received a Form FDA 483, "Inspectional Observations," that listed the deviations noted and those deviations were discussed with him. The violations noted during this inspection include the following:



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1. Failure to adhere to the general responsibilities of a sponsor, including failure to secure investigator compliance, ensure Institutional Review Board (IRB) review and approval, and select qualified investigators (21 CFR 812.40, 812.42, 812.43(a), and 812.46).

You failed to obtain IRB approval prior to starting an investigational study and failed to ensure that investigators participating in these studies obtained IRB review and approval. Robert Y. Jones stated that he did not know whether IRBs were utilized in the conduct of these clinical studies. If IRBs were utilized, Mr. Jones did not know the names of the IRBs responsible for reviewing and approving the protocols and the informed consent. Furthermore, he did not know whether one of the clinical investigators, Dr. Jerry E. Bouquot, Morgantown, West Virginia, obtained IRB approval prior to enrolling subjects. Because Robert Y. Jones could not confirm the use of IRBs for these studies and there were no records indicating such use, we have concluded that IRB approval was not obtained prior to the start of these studies.

Also, you failed to ensure proper monitoring of the investigations. There were no records of Cavitat's monitoring procedures or monitoring visits.

You also failed to select investigators qualified by training and experience to investigate the device. For example, Dr. Bouquot was identified as the Principal Investigator for the two investigational studies. However, Robert Y. Jones did not know the individuals who had been identified by Dr. Bouquot as Sub-Investigators -- Drs. Wesley E. Shankland, Michael Margolis, and Jacques Imbea -- or whether Dr. Bouquot evaluated the Sub-Investigators participating in the study for qualification and clinical experience. The Sub-Investigators sent radiographs, Cavitat scans, clinical information, and bone biopsies, when applicable, to Dr. Bouquot for evaluation.

In addition, you failed to obtain a signed investigator's agreement from each participating investigator, which should have included the investigator's curriculum vitae, a statement of the investigator's relevant experience (including dates, location, extent, and type of experience), and a statement of the investigator's commitment to conduct the investigation in accordance with the agreement (including the investigational plan, the conditions of approval imposed by the reviewing IRB, and a commitment to supervise all testing of the device involving human subjects and to ensure that the requirements of obtaining informed consent were met). Robert Y. Jones stated that he was not aware of the Sponsor regulation associated with Investigator Agreements and that he was unaware that any investigator agreements existed for the two Cavitat studies.

2. Failure to establish an investigational plan and provide investigators with information necessary to conduct the investigation (21 CFR 812.25 and 812.45).

Robert Y. Jones stated that Cavitat did not establish an investigational plan associated with the two studies because you did not consider Cavitat to be the Sponsor of the study. The firm believed that these responsibilities fell to Dr. Bouquot in West Virginia, since he was conducting the study. According to Robert Y. Jones, IRB approval for the protocol and the

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informed consent was also to be secured by Dr. Bouquot. Dr. Bouquot, however, was not even aware that he was conducting an investigational study. FDA's regulations require the study sponsor to provide investigators with the information they need to properly conduct the study including an investigational plan. We acknowledge Robert Y. Jones's verbal response that Cavitat provided several promotional and instructional items to the sub-investigators for use in conducting the studies, but those materials were insufficient to meet the sponsor's responsibilities under FDA's regulations.

In addition, Cavitat did not perform a risk analysis which should have included a description and analysis of all increased risks to which subjects would be exposed by the investigation and the manner in which these risks would be minimized.

3. Failure to maintain accurate, complete, and current records (21 CFR 812.140)

You failed to maintain documentation showing the shipment and disposition of the investigational devices. There is no documentation to show that investigational devices were provided to only qualified investigators participating in the study. Robert Y. Jones stated that Cavitat does not have a device accountability log and that has not maintained a record to account for the locations to which the investigational devices were shipped prior to 510(k) clearance on February 15, 2002. He recalled that the firm shipped approximately 6 devices for investigational use prior to approval, but there is no documentation to support this recollection.

Also, you failed to maintain a copy of Dr. Bouquot's Curriculum Vitae (CV). Investigator Medina requested a copy of Dr. Bouquot's CV during the inspection, and it was provided to her by Sarah J. Jones, Executive Vice President of Administration. Mrs. Jones obtained the CV from the Internet, and it was dated November 4, 2002, which is after the 510(k) clearance date of February 15, 2002. As the sponsor, you should have obtained Dr. Bouquot's CV prior to the start of the study and maintained it in Cavitat's records.

The deviations listed above are not intended to be an all-inclusive list of deficiencies that may exist in these clinical studies.

We note that Robert Y. Jones provided a verbal response to each of the items listed on the FDA Form 483 and stated that steps have been implemented to prevent future violations. He did not specify the corrective steps you plan to take and how you would prevent future deviations. In general, his explanations indicated a lack of understanding of the regulatory requirements that sponsors must meet and included few corrective actions taken or planned. It is important for a sponsor to understand that, unless the physical safety of a subject demands otherwise, treatment of study subjects must adhere to the requirements of the investigational plan.

Enclosed to assist you in better understanding your responsibilities as a sponsor are copies of 21 CFR Parts 50, 54, 56 and 812. These documents also are available electronically, at www.access.gpo.gov/nara/cfr. Part 812 describes your responsibilities as a sponsor of a study of investigational medical devices, and Part 50 includes what is required to protect the welfare of study subjects. Part 54, Financial Disclosure by Clinical Investigators, includes

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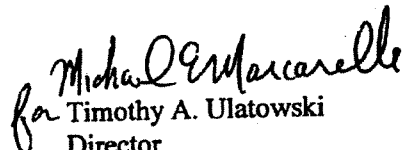
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information regarding your regulatory responsibilities with regard to the welfare of study subjects and responsibilities with regard to any financial interest you might have in the outcome of studies in which you participate. Part 56, Institutional Review Boards, covers the responsibilities of IRBs and sponsors.

Please inform us, **within 15 working days** of receipt of this letter, of the additional corrective actions you have taken or plan to take with regard to the deviations noted. In your response, please explain the roles of Drs. Shankland, Margolis, and Imbeau in the studies, as we did not get an adequate response on this point from Robert Y. Jones. Please send your response 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: D.L. Bernato. Failure to respond could result in regulatory action without further notice.

A copy of this letter has been sent to FDA's Denver District Office, Denver Federal Center Bldg. 20, P.O. Box 25087, 6th Ave. & Kipling Street, Denver, Colorado 80225. If you have any questions, feel free to contact D. Laurie Bernato at (301) 594-4719, ext. 129

Sincerely yours,


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

Enclosures

cc:

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