



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Public Health Service

MAY 14 2004

WARNING LETTER

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

Via Federal Express

Robert W. Churinetz
Senior Vice President
Wright Medical Technology, Inc.
5677 Airline Rd.
Arlington, TN 38002-0100

Dear Mr. Churinetz:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at Wright Medical Technology, Incorporated. This letter also requests that you implement prompt corrective actions. Ms. Emily E. Smith, an Investigator from FDA's New Orleans District Office, conducted the inspection from January 20 through January 29, 2004. The purpose of the inspection was to determine if your activities as a Sponsor of the study for the [REDACTED], PMA # [REDACTED] and IDE # [REDACTED] complied with applicable FDA regulations. The products used in the study are devices as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321(h)].

The FDA 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. The program also ensures that human subjects are protected from undue hazard or risk during the course of scientific investigation.

Our review of the inspection report and related documents submitted by the New Orleans District Office revealed serious violations of Title 21, Code of Federal Regulations, (21 CFR), Part 812 – Investigational Device Exemptions, and Section 520(g) of the Act [21 U.S.C. 360j(g)]. At the close of the inspection, Ms. Smith discussed deviations observed during this inspection with Roger Brown, Kate Garretson, and Becky Fortner. The deviations noted during the inspection and our subsequent inspection report review are discussed below:

Failure to ensure proper monitoring of the investigation and failure to secure investigator compliance [21 CFR 812.40 and 46(a)].

Examples of these failures include but are not limited to the following:

- The Investigational Plan you submitted to the FDA under IDE [REDACTED] stated that “Monitoring visits will be conducted as needed but at least annually.” Your records showed that, of the ten study sites participating in the study, four have not received a monitoring visit since 2002. Specifically:

- Dr. [REDACTED]--the last monitoring visit was June 3-5, 2002.
- Dr. [REDACTED]--the last monitoring visit was February 15, 2002.
- Dr. [REDACTED]--the last monitoring visit was December 5, 2002.
- Dr. [REDACTED]--the last monitoring visit was February 4, 2002.

All four of these clinical investigators are continuing to collect safety and efficacy study data from enrolled subjects, even though the study may be closed to active enrollment. Responsibilities of Sponsors include ensuring proper monitoring of the investigation [21 CFR 812.40] in order to secure compliance with the investigational plan [21 CFR 812.46(a)]. In addition, since these clinical sites have not been monitored since 2002, the study data reported to the FDA in your PMA submission, [REDACTED], have not been verified against the subjects’ case histories maintained by the clinical investigators.

- A sponsor who discovers that an investigator is not complying with the signed investigator agreement, the investigational plan, the requirements of applicable FDA regulations, or any conditions of approval imposed by FDA or the reviewing Institutional Review Board (IRB) must promptly either secure compliance or discontinue shipments of the device to the investigator and terminate the investigator’s participation in the investigation [21 CFR 812.46].

Your records contained documentation of several protocol deviations by clinical investigators participating in the study for IDE [REDACTED], yet you failed to secure investigator compliance. Examples of these failures include the following:

- Dr. [REDACTED] deviated from the protocol by not using the test article in at least three subjects. Two of these subjects, [REDACTED] and [REDACTED], received a hip component from another company’s device and are included in the primary efficacy data analysis reported to the FDA in your PMA submission (P[REDACTED]).
- Dr. [REDACTED] and Dr. [REDACTED] (site [REDACTED]) each enrolled at least one subject who did not meet eligibility criteria. Both of these subjects, [REDACTED] and [REDACTED], are included in the primary efficacy data analysis reported to the FDA in your PMA submission (P[REDACTED]).

- Dr. [REDACTED] (site [REDACTED]) enrolled eleven patients whose range of motion efficacy data had to be deleted from the database because there was no record that Dr. [REDACTED] had actually seen the patients.
- There were numerous instances across several clinical sites of study patients with missed post-surgical follow-up visits and follow-up evaluations.

There were no records to demonstrate that your firm obtained prompt correction and subsequent compliance by the clinical investigators in question, or that your firm terminated the clinical investigator's participation in the study to prevent the recurrence of serious protocol deviations or regulatory violations.

Failure to report all adverse events that occurred during the study to the FDA as required by 520(g) of Act.

An example of this failure includes but is not limited to the following:

A requirement of the IDE approval that you received for this device study is that you make reports to the FDA of data obtained as a result of the investigational use of the device during this study. This includes reporting adverse events. This information assists the FDA in determining compliance with the conditions granted, reviewing the progress of the investigation, and evaluating the safety and effectiveness of the device. The Investigational Plan you submitted to the FDA under IDE [REDACTED] stated that all adverse events and complications that occurred at the study sites would be reported to the FDA. However, at least four serious adverse events that occurred at Clinical Study site [REDACTED] between 2001 and 2003 were not reported to the FDA:

- Pt. [REDACTED]: Dislocation of the device requiring closed reduction on 6/6/01. This event was considered to be possibly related to the study device by the clinical investigator.
- Pt. [REDACTED]: Grade II – III heterotopic ossification of the right hip, diagnosed 5/9/02, and Grade III heterotopic ossification of the right hip diagnosed on 5/21/03. These events were recorded at the subject's follow-up visits, but were not reported on an Adverse Event Form as required by the study protocol.
- Pt. [REDACTED]: Cardiac catheterization and insertion of stents for treatment of coronary artery disease on 12/11/01. This event was considered to be unrelated to the study device by the clinical investigator.
- Pt. [REDACTED]: Surgical removal of tonsils and section of uvula for treatment of obstructive sleep apnea on 6/6/02. This event was considered to be unrelated to the study device by the clinical investigator.

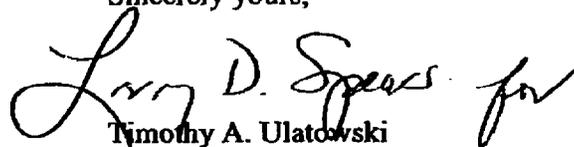
The above-described deviations are not intended to be an all-inclusive list of deficiencies that may exist in this clinical study. It is your responsibility as a sponsor to assure adherence to each requirement of the Act and all pertinent federal regulations.

Within 15 working days after receiving this letter, please provide written documentation of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies. 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:

Food and Drug Administration
Center for Devices and Radiological Health, Office of Compliance
Division of Bioresearch Monitoring, Program Enforcement Branch II, HFZ-312
2094 Gaither Road, Rockville, Maryland 20850
Attn: Mr. Levering Keely, Consumer Safety Officer.

We are also sending a copy of this letter to FDA's New Orleans District Office, Food and Drug Administration, 22201 23rd Drive SE, Bothell, WA 98021. We request that you also send a copy of your response to that office. If you have any questions, please contact Mr. Keely by phone at 301-594-4720, ext. 142, or by e-mail at Levering_Keely@fda.hhs.gov.

Sincerely yours,

A handwritten signature in black ink that reads "Timothy A. Ulatowski" followed by a stylized flourish.

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