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Food and Drug Administration
2098 Gaither Road
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WARNING LETTER

FEDERAL EXPRESS

Patrick A. Abbey, D.M.D., P.A.
Maxillofacial Surgery Center
3000 E. Fletcher Avenue, Suite 100
Tampa, Florida 33613-4613

Dear Dr. Abbey:

During the period of June 21 through June 28, 1999, Mr. Michael W. Roosevelt and Ms. Christine M. Humphrey, investigators with the Food and Drug Administration (FDA), Florida District Office, conducted an inspection at your facility. The purpose of that inspection was to determine whether your activities and procedures as a clinical investigator of the investigational study of the [REDACTED] complied with applicable FDA regulations. These products are devices as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

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 Notifications [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 submitted by the District Office revealed that there were significant violations 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, Mr. Roosevelt and Ms. Humphrey presented to and discussed with you the observations listed on the Form FDA-483, "Inspectional Observations." [REDACTED], Office Manager, and [REDACTED], Surgical Assistant, were present throughout the inspection and provided pertinent information. The following list of violations is not intended to be an all-inclusive list of deficiencies in the above referenced clinical study:

Failure to obtain informed consent in accordance with 21 CFR Part 50.20 and to report to the Sponsor within 5 days the use of the device without obtaining informed consent [21 CFR Part 812.150(a)(5)].

- You failed to obtain study subjects informed consent prior to surgery. For example, [REDACTED] had surgery on 1/8/97 and the consent was signed on 5/01/97; [REDACTED] had surgery on 9/2/97 and the consent was signed on 10/27/97; and [REDACTED] had surgery on 7/27/98 and the consent was signed on 6/15/98.
- You failed to obtain informed consent from [REDACTED]
- You failed to obtain a signature and date on the informed consent form for [REDACTED] the consent contained initials only.

21 CFR Part 50.20 states that no investigator may involve a human being as a subject in research unless the investigator has obtained informed consent from the subject or from the subject's legally authorized representative. Also, 21 CFR 50.20 requires that an investigator obtain the study subjects' informed consent under circumstances that provide the prospective subject sufficient opportunity to consider whether or not to participate in the study and under circumstances that minimizes the possibility of coercion or undue influence. Further, if an investigator uses a device without obtaining informed consent, this must be reported within 5 days after the use to the Sponsor and the reviewing IRB.

Failure to obtain IRB and FDA approval before allowing subjects to participate in the study as required by 21 CFR 812.110(a).

- Your study lacked IRB approval during the period of 11/01/97 through 01/22/98 and from 05/01/98 through 06/25/98. In addition, there is no documentation to indicate IRB approval of the study from 11/01/98 to the present.

Failure to prepare and submit complete, accurate, and timely adverse event reports as required by 21 CFR 812.150(a)(1).

You failed to report adverse events to the sponsor and IRB, for example:

- [REDACTED] adverse event page had a yellow post-it note attached which read, "1/14 swollen pain lock jaw" and "1/18 admitted for infect." The subject's medical records describe events such as facial swelling, pain, and seizure which were not reported to the sponsor.
- [REDACTED] underwent a total of three study surgeries (9/2/97, 11/2/98, and 3/23/98); the third surgery was performed to reposition the [REDACTED] which had become dislocated. Case report and adverse event forms for this surgery were not completed and submitted to the sponsor or the IRB.

Failure to conduct the investigation in accordance with the investigational plan [21 CFR 812.110(b)].

You failed to follow the study protocol in that follow-up visits for some subjects were not conducted on schedule or, for some, not conducted at all. Also, required x-rays were not taken. For example:

- Visit 4, for [REDACTED], was conducted one month too early. The surgery date for this subject was 1/8/97; therefore, the date for visit 4 should have been 6/8/97. In addition, visits 5 and 7 for this subject were not conducted. Also, panoramic x-rays were not taken at visits 4 and 6, as required by the protocol.
- [REDACTED] was not physically examined during visit 6. This visit was conducted by telephone; therefore, the range of motion values recorded, on the case report form, were not actually measured but were based on the patient stating that her mouth opening had not changed since her last office visit.
- Panoramic x-rays for [REDACTED] were not taken during visit 5, as required by the protocol. Further, the subject's medical record dated 10/26/98 indicates that the subject was in the office for the one-year follow-up, but an exam was not conducted at that time.
- Panoramic x-rays for [REDACTED] were not taken during visit 4, as required by the protocol.

Failure to maintain adequate, complete, and current records [21 CFR 812.140].

- There is no source documentation for [REDACTED] for the dentofacial clinical exam range of motion values for Visit 1.
- The subject symptom assessment form for [REDACTED] was not completed during visits 2 and 3, and there is no source documentation for dentofacial clinical exam range of motion values for Visit 1.
- There is no source documentation for [REDACTED] for dentofacial clinical exam range of motion values for visit 1. Further, records for this subject indicate that visit 4 was conducted on 4/16/98, but the case report forms are dated 4/10/97. The dentofacial clinical exam range of motion value for this visit was recorded in the patient medical chart as 26mm; this does not correspond with the value of 24mm reported in the case report form. Notes from the sponsor monitor visit indicate that the case report form for the subject symptom assessment was not completed during this visit. This form should be completed by the study subject during each visit.

In addition, at visit 5, the dentofacial clinical exam range of motion value for this subject was recorded in the medical chart as 21-32mm; this does not correspond with the value of 24-31mm reported in the case report form.

- Visit 6, for [REDACTED] was recorded on the case report form for visit 5. The dentofacial clinical exam range of motion value for this visit was recorded in the medical charts as 33mm; this does not correspond with the value of 32mm reported in the case report form.
- Visit 3, [REDACTED] was conducted on 2/4/98, but there is no documentation in the patient medical chart or case report forms of any visits for this subject after 2/4/98; yet, the case report form for early discontinuation was not completed. Further, there is no source documentation for this subject for the dentofacial clinical exam range of motion values for Visit 1.
- Case report forms were not completed for [REDACTED] Visit 2 (post-op) for this subject was conducted on 1/12/98. The patient medical chart indicates that the most recent contact with the study subject was 5/21/98; yet the case report form for early discontinuation was not completed.

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- The case report form for the subject symptom assessment for [REDACTED] visit 3, is not dated. Further, there is no source documentation for this subject for the dentofacial clinical exam range of motion values for Visit 1.

As an investigator, it is your responsibility to ensure that your investigation is conducted in accordance with the signed agreement, the investigational plan, and applicable FDA regulations. This includes adequate and accurate recordkeeping as well as the reporting of all adverse device events.

Please advise this office, in writing, within 15 working days of receipt of this letter, of the specific steps you have taken or will be taking to correct these violations and to prevent the recurrence of similar violations in current or future studies. 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: Pamela Reynolds. A copy of this letter has been forwarded to our Florida District Office, 555 Winderley Place, Suite 200, Maitland, Florida 32751. We request that a copy of your response be sent to that office.

If you have any questions or concerns, feel free to contact Ms. Pamela Reynolds at (301) 594-4720, ext. 155.

Sincerely yours,



Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health