



g4655d

via Federal Express

APR 23 2004

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

WARNING LETTER

Mr. David Bailey  
President and CEO  
STAAR Surgical  
1911 Walker Avenue  
Monrovia, California 91016

Dear Mr. Bailey:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at STAAR Surgical. This letter also discusses the January 6, 2004, written response from Helene Lamielle, M.D., Vice President of Scientific Affairs, STAAR Surgical, to FDA in response to the violations noted, and request that STAAR Surgical implement prompt corrective actions. Ms. Deborah A. Greco and Ms. Jocelyn E. Sparks, investigators from the FDA's Los Angeles District Office, conducted the inspection from December 3 through December 11, 2003. The purpose of the inspection was to determine if your activities as a Sponsor/Monitor for the [REDACTED] study complied with applicable FDA regulations. The [REDACTED] is a device as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 321(h)].

The FDA conducted the inspection 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 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, Ms. Greco and Ms. Sparks presented a Form FDA 483, "Inspectional Observations," to Dr. Lamielle and discussed the listed deviations with her. Also participating in this discussion of the listed deviations were

[REDACTED]

The deviations noted on the Form FDA 483 and our subsequent review of the inspection report, as well as Dr. Lamielle's response to the Form FDA 483 items, are discussed below. Unless otherwise stated, Dr. Lamielle's responses to the noted deviations are adequate.

***Failure to obtain FDA approval prior to initiating the study (21 CFR 812.20(a)(1) and (2) 812.40, and 812.42).***

STAAR Surgical provided the investigational device to [REDACTED] prior to FDA approval. FDA conditionally approved the IDE in January 2002. FDA's review of correspondence dated July 5, 2001, from STAAR Surgical to Dr. [REDACTED] revealed that STAAR Surgical provided Dr. [REDACTED] with the investigational device on [REDACTED].

- Dr. Lamielle's response acknowledges this observation and states that STAAR Surgical's former Vice President of Regulatory Affairs [REDACTED] misinterpreted FDA regulations regarding custom-devices and provided two [REDACTED] devices to a clinical investigator to be implanted; however, once the firm's [REDACTED] became aware of this, she requested that the devices be returned to STAAR and not be implanted until FDA approval of the IDE.
- Dr. Lamielle's response also states that the [REDACTED] of STAAR Surgical (the patient for whom the [REDACTED] was intended) and the Vice President of Regulatory Affairs are no longer employed by STAAR Surgical.
- Dr. Lamielle's response further states that procedures for [REDACTED] were revised in [REDACTED] and that all members of the [REDACTED], as well as members of the [REDACTED] and [REDACTED] and all other relevant personnel, will attend training sessions regarding [REDACTED] to ensure that they are fully educated regarding devices intended for use in IDE clinical trials with emphasis on the fact that investigational devices may only be shipped to designated [REDACTED] personnel "or to a site specified by those personnel and not to any other individual within or without the organization."

These corrective actions appear adequate. However, the fact remains that the devices were shipped to be implanted prior to FDA approval. FDA regulations clearly state that a sponsor shall submit an application to FDA if the sponsor intends to use a significant risk device in an investigation, and may not begin an

investigation for which FDA's approval of an application is required until FDA has approved the application.

***Failure to obtain continuing IRB review (21 CFR 812.40 and 21 CFR 812.40).***

STAAR Surgical failed to ensure that continuing IRB review was received prior to continuation of the study. There was no documentation to indicate that the IRB met and approved the continuation of the study located at [REDACTED] for the period of 1999 through 2000. IRB approval is required prior to initiation of any investigational study involving an FDA-regulated product.

Dr. Lamielle's response states that this was an isolated occurrence and that your [REDACTED] contains a retraining provision for all [REDACTED] personnel, as well as any contract monitoring personnel, to reemphasize the requirement for, and importance of, ensuring that IRB continuing review and approval is performed for all sites on an annual basis.

***Failure to comply with sponsor responsibilities (21 CFR 812.40 and 21 CFR 812.43(c)).***

Examples of this failure include, but are not limited to, the following:

- FDA regulations require the sponsor to obtain a signed agreement from each participating investigator prior to his or her participation in the study. A monitoring report dated [REDACTED], revealed that [REDACTED] was asked by a STAAR Surgical employee to back-date an investigator's agreement. Investigator agreements should be signed prior to the investigator's participation in the study. The investigator's agreement is important because it is a statement of the investigator's commitment to conduct the investigation in accordance with the investigational plan, FDA regulations, and any conditions imposed by the reviewing IRB and FDA.

Dr. Lamielle's response states that STAAR Surgical's procedure for [REDACTED] has been revised to more clearly state the requirement for obtaining signed investigator's agreements prior to the commencement of any clinical trial at any investigational site, and that members of the [REDACTED] and relevant personnel from the [REDACTED] will be trained in the revised procedure as appropriate.

- STAAR Surgical failed to identify all exclusion criteria on the [REDACTED]. For example, one of the exclusion criteria listed in the protocol was that study subjects must not be insulin dependent diabetics. However, this criterion was not listed on the patients' eligibility checklists. Furthermore, there was no documentation in the patient files reviewed by our inspectors that would confirm whether or not patients were insulin dependent diabetics. As the sponsor, you are responsible for providing investigators the information they need to conduct the investigation in accordance with the protocol.

Dr. Lamielle's response states that each site has been contacted to confirm that no insulin dependent diabetic patients were enrolled in the study and that all eligibility checklists leaving the Sponsor as of this date include the criterion for insulin dependent diabetics. In addition, you plan to implement an SOP that defines the requirements and responsibilities for eligibility checklists as well as other required documentation to ensure that these meet protocol requirements.

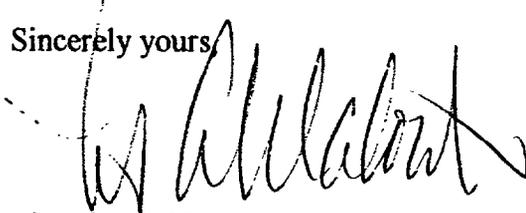
The above described deviations are not intended to be an all-inclusive list of deficiencies that may exist in your clinical study. It is your responsibility as a sponsor to assure adherence to each requirement of the Act and all applicable federal regulations. Dr. Lamielle's response indicates that STAAR Surgical has developed corrective measures and implemented new procedures including new and revised SOPs to ensure that these deviations are not repeated in the future.

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

Page 5 - Mr. David Bailey

We are also sending a copy of this letter to FDA's Los Angeles District Office, 19900 MacArthur Blvd., Suite 300, Irvine, California 92612. We request that you also send a copy of your response to that office. If you have any questions about this letter, please contact Ms. Reynolds at (311)594-4720, or by e-mail at [pmr@cdrh.fda.gov](mailto:pmr@cdrh.fda.gov).

Sincerely yours,



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

cc: Helene Lamielle, M.D.  
Vice President  
Scientific Affairs  
STAAR Surgical Company, Inc.  
1911 Walker Avenue  
Monrovia, California 91016