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

WARNING LETTER
Via Federal Express

Sam B. Humphries, President & CEO
Uroplasty, Inc.
2718 Summer Street NE
Minneapolis, Minnesota 55413-2820

Dear Mr. Humphries:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your firm during the period of March 8 through 29, 2005. The inspection was conducted by investigators with FDA's Minneapolis District Office. This letter also discusses the April 19 response to the Form FDA 483, "Inspectional Observations," from Michael Morrell, the Director of Regulatory Affairs at your firm, and requests that you implement prompt corrective actions. The purpose of the inspection was to determine if your activities as the sponsor of a study involving the [REDACTED] complied with applicable FDA regulations. [REDACTED] 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 (PMA) applications, 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 prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812, Investigational Device Exemptions; Part 50, Protection of Human Subjects; and Part 814, Premarket Approval of Medical Devices. At the close of the inspection the FDA investigators presented a Form FDA 483 to Susan Hartjes Holman, Uroplasty's Chief Operating Officer, for review and discussed the listed deviations with Ms. Holman, Mr. Morrell, and [REDACTED]. The deviations noted on the Form FDA 483, Mr. Morrell's response, and our subsequent inspection report review are discussed below.

Failure to ensure adequate monitoring of an investigational study [21 CFR 812.40]

Pursuant to 21 CFR 812.40, sponsors are responsible for ensuring proper monitoring of the investigation. An example of your failure to satisfy the requirement to ensure proper monitoring includes, but is not limited to, the following:

The inspectional report notes that review of subject records across five (5) investigational sites revealed that study procedures were initiated on 30 subjects prior to obtaining the informed consent of these individuals as required by the regulations at 21 CFR Part 50. The inspectional report further notes that the main study monitor, Jeanne Colburn-Sinn, stated during the inspection that the deviation observed is attributable to the fact that monitors only reviewed study records to ensure informed consents were signed prior to the implant procedure, without considering the timing of other study-specific procedures. She further stated that it was not discovered that some study procedures were conducted prior to obtaining informed consent until Clindex software was implemented by Uroplasty in 2004. This software was written to uncover protocol deviations.

Mr. Morrell's response indicates that these protocol deviations were included in the PMA submitted to FDA in December 2004 since the company had documented these instances of conducting study procedures prior to informed consent as deviations. He also states that Uroplasty's Monitoring Standard Operating Procedure (SOP) and Monitoring Checklist will be updated to ensure that in the future monitoring visits will specifically evaluate the informed consent date with the dates of baseline screening. In addition, he states that your clinical protocol SOP will be updated to ensure that future study protocols provide specific instructions as to when each investigational site must obtain informed consent from potential study subjects. We are also aware that Uroplasty has submitted an audit plan to the Office of Device Evaluation for their review and consideration. These corrective actions are appropriate.

Failure to ensure that investigators comply with the signed agreement, the investigational plan, the requirements of Part 812 or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA. [21 CFR 812.46(a)]

Under FDA regulations, upon discovering that an investigator is not complying with the investigational plan, a sponsor is required either to promptly secure compliance or discontinue shipments of the device to the investigator and terminate the investigator's participation. Examples of your failure to satisfy this requirement include, but are not limited to, the following:

The inspectional report notes that the twelve-month [REDACTED] examination was not routinely performed at site 11, [REDACTED] as required by the investigational plan. According to the inspection report, [REDACTED], the clinical investigator at this site, had recommended and requested in correspondence dated [REDACTED] that the [REDACTED] at the twelve-month follow-up visit be

eliminated from the protocol by the sponsor for all subjects who required no further [REDACTED] treatment at that time. According to the reviewing division in FDA's Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), in [REDACTED] Uroplasty withdrew an IDE supplement requesting removal of the requirement that [REDACTED] be performed at the twelve-month visit after ODE determined that the examination was necessary. Inspectional findings revealed that Uroplasty informed [REDACTED] of ODE's decision in a [REDACTED] memorandum. Because the first subject was treated at site 11 on [REDACTED], this memorandum was sent well before any of the subjects at the site reached their first twelve-month follow-up date in [REDACTED]. Nevertheless, site 11 had 35 out of 40 subjects who did not receive the twelve-month follow-up [REDACTED] examination as required by protocol, with 25 subjects noted as refusing the examination or having it performed outside of the prescribed window and 10 others exiting the study prior to this visit. Mr. Morrell's response states that failure to routinely do [REDACTED] testing at this site at this follow-up visit was reported to FDA in the annual progress reports as protocol deviations. However, there was no indication that Uroplasty attempted to ensure that the remaining subjects at this site had a [REDACTED] performed, or to terminate the investigator's participation if it was determined he would not abide by this requirement.

Mr. Morrell's response states that to terminate [REDACTED] participation would be self-defeating for all parties, since it potentially denies [REDACTED] subjects continued follow-up and results in unnecessary loss of data to the sponsor. If [REDACTED] refused to complete follow-up visits as required by the protocol, then Uroplasty could have solicited the participation of another qualified practitioner who was willing to follow the protocol-required follow-up testing regime and complete the corresponding case report forms (CRFs). Not obtaining compliance with this protocol requirement resulted in incomplete data on the subjects who failed to have the procedure and potentially placed them at risk, as it was not known before the completion of the study whether a twelve-month [REDACTED] examination was necessary to reveal potential adverse effects.

As a corrective action for future investigations, Mr. Morrell's response states that Uroplasty's SOP for Preventative/Corrective Action will establish a procedure to identify the type and frequency of protocol deviations to be specifically monitored on a regular basis during the course of the study. In addition, he states that frequent protocol deviations will result in an automatic letter to the investigator documenting the issues and requesting immediate compliance. This is an appropriate corrective action.

Failure to report all adverse reactions and complications in the PMA application (21 CFR 814.20(b)(6)(ii))

A PMA applicant is required by 21 CFR 814.20(b)(6)(ii) to report all information regarding the results of a clinical investigation including all adverse reactions and complications. Examples of your failure to satisfy this requirement include, but are not limited to, the following:

Investigational findings revealed that adverse reactions that occurred during the first 48 hours [REDACTED] were not reported in the PMA. Mr. Morrell's response notes that these transient symptoms were expected and that Uroplasty followed the example of [REDACTED] as evidenced in their Summary of Safety and Effectiveness section in which they separated adverse effects from transient symptoms. However, as seen in the [REDACTED] example that was included in the response, their transient symptoms were reported, even though they were reported separately from the adverse effects.

Mr. Morrell states that the missing transient symptom information will be submitted to FDA as an amendment to the PMA. He also states that Uroplasty's SOP for the creation of clinical protocols will be amended to assure the inclusion of specific instructions regarding the reporting of adverse effects for a study and also will describe how such effects will be analyzed during the study. This is an appropriate corrective action plan.

Failure to have an adequate investigator agreement (21 CFR 812.43(c))

Pursuant to 21 CFR 812.43(c), a sponsor shall obtain from each participating investigator a signed agreement that includes sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement to FDA. The agreement also must contain a commitment from the investigator to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following the completion of the study. Examples of your failure to satisfy this requirement include, but are not limited to, the following:

Inspectional findings indicate that financial disclosure information for the investigators participating in the [REDACTED] study was not collected until [REDACTED], shortly before the submission of the PMA in [REDACTED]. Because the financial disclosure forms were not signed until late in the study, they lacked a commitment to update this information "during the course of the investigation" as required by 21 CFR 812.43(c)(5).

Mr. Morrell's response states that Uroplasty's SOP for Clinical Trial Agreements will be amended to add a statement that the collection of financial disclosure information is a required element of an investigator agreement. This is an appropriate corrective action.

In addition to the observations noted on the Form FDA 483, the FDA investigator discussed with Ms. Holman the fact that a number of protocol deviations were not identified until late in the study when it was too late to take actions to prevent their recurrence. The inspection report notes that Ms. Holman replied that the Clindex program, which was not brought on-line until the summer of 2004, did manage to identify a number of deviations not previously noted. The FDA investigator also noted that it is the sponsor's responsibility to ensure monitoring is adequate to reveal protocol deviations in a timely manner rather than to depend only on software analysis of the data, particularly since this software was not available for most of the study.

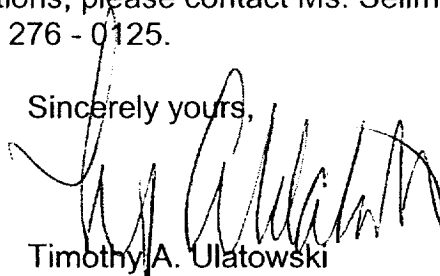
A separate inspection of the [REDACTED] site also revealed that monitors were completing anticipated adverse event logs for the study (copies enclosed). Please note that forms containing study data should not be completed by study monitors or other personnel outside of the site study team. Only clinical investigators and appropriately delegated members of the site study team should complete forms with study data.

The deviations described above are not intended to be an all-inclusive list of deficiencies that may have occurred in connection with this study. It is your responsibility as a sponsor to comply with applicable regulations.

Within fifteen (15) working days after receiving this letter please respond in writing with a description of any corrective actions your firm has taken or will take with regard to those items discussed above that were not included in Mr. Morrell's response to the Form FDA 483 observations. In addition, please provide us with copies of the amendments to Uroplasty's SOPs that were discussed as corrective actions in Mr. Morrell's response. If amendment of these SOPs is not yet complete, please provide an estimate as to when we will receive them. Failure to respond to this letter and take appropriate corrective action could result in FDA taking regulatory action without further notice to you. Please send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Viola Sellman, Branch Chief.

We are sending a copy of this letter to FDA's Minneapolis District Office, 240 Hennepin Avenue, Minneapolis, Minnesota 55401, and request that you also send a copy of your response to that office. If you have any questions, please contact Ms. Sellman at the address listed above or by telephone at (240) 276 - 0125.

Sincerely yours,



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

Enclosures