Inspections, Compliance, Enforcement, and Criminal Investigations

Instrumed Gmbh 3/28/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

March 28, 2014

WARNING LETTER

VIA UNITED PARCEL SERVICE

Peter E. Fetzer
Managing Director, Owner
Instrumed GmBH
Unter Buchsteig 3
D- 78532 Tuttlingen, Germany

Dear Mr. Fetzer:

During an inspection of your firm located in Tuttlingen, Germany on July 29, 2013, through August 01, 2013, investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures medical devices including, but not limited to: laparoscopes, surgical clamps, vascular and thoracic suction tubes, surgical knives, and vascular wire retractors. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received a response from Forrest Whittaker, CEO, Avalign Technologies, dated September 13, 2013, and October 28, 2013, concerning our investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations, that was issued to your firm. We address this response below, in relation to each of the noted violations. We also received a response from Mr. Whittaker dated December 26, 2013, which has not been reviewed. These violations include, but are not limited to, the following:

1. Failure to establish and maintain design validation procedures to ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions, as required by 21 CFR 820.30(g). For example, your firm's design validation practice is inadequate. Specifically, the IFU for Right Angle Electrodes from your contract manufacturer includes a voltage warning stating that any voltage exceeding 650Vp could lead to tissue damage. Right Angle Electrodes are included as part of your firm's finished device. However, the IFU included in the finished device does not have the voltage warning. According to your firm's complaint record, the lack of warning has led to users using the product at a high voltage, causing melting or tip damage and, in some cases, patient injury. Your firm's classified these complaints as "user error". However, your firm design validation failed to consider the conditions similar to those that are expected to be experienced in the user environment, the actual conditions of use, or how the lack of explicit instructions could lead to device malfunction or injury to the patient.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response indicated that all labeling will be reviewed to ensure consistency. Your firm's response indicated that your firm has notified its customer (**(b)(4)**) to update the label to include maximum power settings specified in the 510(k). Your firm is currently awaiting confirmation from **(b)(4)** and plans to complete labeling updates by February 15, 2014. Your firm should perform a risk assessment to determine whether correction or removal is necessary for the affected products.

2. Failure to establish and maintain procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a). For example:

a. Your firm failed to identify actions needed to correct and prevent recurrence of nonconforming products. Specifically, your firm identified that **(b)(4)** of all **(b)(4)** complaints for laparoscopic devices are related to insulation damages and cracking issues and **(b)(4)** of all **(b)(4)** complaints are related to sterilization/cleaning issues. However, your firm did not initiate a corrective action to reduce re-occurrence of either issue.

b. Your firm failed to comply with its correction and prevention action (CAPA) procedure, Avalign CAPA, CORP_SOP-0024. The procedure requires an escalation of a corrective action when a supplier issues **(b)(4)** CAPA reports over a **(b)(4)** period. Your firm had multiple suppliers which met this criteria, but failed to issue CAPAs. Your firm did not document justifications for not opening a CAPA.

c. Your firm initiated multiple CAPAs for Frazier and Baron suction tubes that were cracking due to poor attachment. CAPA 2010-09 was initiated on September 27, 2010, to investigate a trend in complaints related to an increased return of suction tubes. The corrective action was to change the method **(b)(4)**. The corrective action was completed and dated February 16, 2011. However, no documentation of the validation of the **(b)(4)** process was documented or referenced in your firm's file. Your firm reopened the CAPA in the first quarter of 2012 and a memo to file, dated February 9, 2012, indicated that **(b)(4)** method was changed to **(b)(4)** method. However, no validation of the **(b)(4)** method was included in the file.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not address the validation issue. Your firm should conduct a risk assessment for the affected devices and determine whether a correction and/or removal are necessary.

3. Failure to establish and maintain procedures for acceptance activities, which include inspections, tests, or other verification activities, as required by 21 CFR 820.80(a). For example, your firm's incoming acceptance activities are inadequate. Specifically, the following deficiencies are noted:

a. Your firm lacked acceptance criteria for the final device acceptance activities. Your firm's inspection plan requires **(b)(4)**. However, specific details related to what to check and what

tools to use were not defined.

b. Your firm's Receiving-Finished Product procedure, D0I-824-P-2, does not state what calibration tools are required to test a specific device.

c. Your firm's inspection reports on file do not include a record of actual measurements for dimensional checks.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not address the above issues; however, your firm considers the observation to be closed without further justification.

4. Failure to establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation, as required by 21 CFR 820.30(b). For example, your firm's design and developmental activities are inadequate. Specifically, at the time of the inspection, your firm did not have design plans available in the DHF for the **(b)(4)** project per your firm's Quality Manual section 7.3.

The adequacy of your firm's response cannot be determined at this time. Your firm plans to retrospectively review Class II products to address the above deficiency. Your firm should confirm that the DHF has been updated to include necessary design plans.

5. Failure to maintain complaint files and establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, as required by 21 CFR 820.198 (a). For example, during the sampling of **(b)(4)** complaint records, none of the complaint records which were not reported as Medical Device Reporting (MDRs) include documentation of the MDR evaluation nor did they document the justification for not reporting.

We reviewed your firm's response and conclude that it is not adequate. Your firm has not performed a review of the complaint files to determine how many complaints are missing required data elements. Your firm has not made an attempt to gather missing required data elements. Your firm has not updated its complaint handling procedures to specify if MDR evaluations will be recorded.

6. Failure to review and evaluate all complaints to determine whether an investigation is necessary and when no investigation is made, maintain a record that includes the reason no investigation was made and the name of the individual responsible for the decision not to investigate, as required by 21 CFR 820.198(b). For example, your firm failed to document the rationale for not investigating a complaint and the individual making the determination in the complaint record.

We reviewed your firm's response and conclude that it is not adequate. Your firm has not performed a review of the complaint files to determine how many complaints are missing the required data elements. Your firm has not made an attempt to gather missing required data elements. Your firm has not documented a decision to not open an investigation on deficient complaints.

7. Failure to validate computer software for its intended use according to an established protocol when computers or automated data processing systems are used as part of production or the quality system, as required by 21 CFR 820.70(i). For example, your firm's **(b)(4)** Software Operating System used to log, evaluate, and investigate complaints, incoming, in process, and finished non-conformances was not validated to prevent deletions of records by employees.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not include a validation report for the Majesty Software Operating System for restricting the deletion of complaints to the Heads of Quality. Additionally, your firm's response did not include

training records on revised procedure.

8. Failure to maintain records of changes to documents to include a description of the change, identification of the affected documents, the signature of the approving individual(s), the approval date, and when the change becomes effective, as required by 21 CFR 820.40(b). For example, your firm claimed to have recently revised its CAPA procedure, SOP-0024, and at the time the CAPA data was compiled, there was no requirement to open a corrective action report based on **(b)(4)**. Your firm's revised CAPA procedure does not show a revision level or revision history to confirm when the procedure was implemented. However, your firm's Document Change Notice #11-057, G-Q-423-F-1, shows that the CAPA procedure was effective as of 2011.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response failed to address the above issues.

9. Failure to establish and maintain procedures to ensure that sampling methods are adequate for their intended use and to ensure that when changes occur the sampling plans are reviewed, as required by 21 CFR 820.250(b). For example, at the time of the inspection, your firm was unable to explain why a sample size of **(b)(4)** units was selected for design validation of **(b)(4)** dated August 2, 2010. Your firm also stated that the sample size of **(b)(4)** units was not based on any valid statistical rationale.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response failed to address the above issues.

10. Failure to establish and maintain procedures to control labeling activities, as required by 21 CFR 820.120. For example, your firm has not established labeling control procedures. Your firm does not have instructions showing how it separates labels and products to prevent mix ups, and how labels are approved. It is unclear how labels are inspected prior to use, and how the signature of the individual performing the inspection is documented in the Device History Record.

We reviewed your firm's response and conclude that it is not adequate. We reviewed your firm's revised Labeling procedure, G-P-765-P-1, which appears to be adequate. Your firm should provide records showing personnel training on the revised procedure.

11. Failure to maintain device master records (DMR's) and to ensure that each DMR is prepared and approved in accordance with 21 CFR 820.40, as required by 21 CFR 820.181. For example, at the time of the inspection, the FDA investigators asked to see all drawings to verify that product specifications were established for each instrument and product. However, your firm's representative was unable to produce specification drawings.

The adequacy of your firm's response cannot be determined at this time. Your firm plans to establish specification drawings for all current surgical devices identifying the required information to inspect and accept a surgical device. All DMRs will be updated to identify the appropriate drawing numbers used to inspect and accept a surgical device. Your firm plans to complete these actions by November 12, 2013. Your firm should provide evidence of implementation of its corrective action.

12. Failure to establish and maintain procedures to ensure that device history records (DHR's) for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the device master record (DMR) and the requirements of 21 CFR 820, as required by 21 CFR 820.184. For example, your firm did not record the number of devices released for distribution on the **(b)(4)** Protocol Sheet. The sheet had a check box for indicating if the test had been conducted, but not the number of products tested and/or released.

We reviewed your firm's response and conclude that it is not adequate. Your firm's response did not address the above issues; however, your firm considers the observation to be closed without

further justification.

Our inspection also revealed that your firm's devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 803 - Medical Device Reporting. Significant violations include, but are not limited to, the following:

1. Failure to adequately develop, maintain and implement written MDR procedures, as required by 21 CFR 803.17. For example, your firm's MDR procedure, MDR Medical Device Reporting/ Vigilance, G-A-851-P-2, revision 2, issued on July 26, 2013, is deficient. Your firm's MDR procedure does not establish internal systems that provide for timely transmission of complete medical device reports as required by 21 CFR 803.17(a)(3). Specifically, your firm's MDR procedure fails to provide the following:

a. Instructions for how to obtain and complete the FDA 3500A form.

b. The timeframe for submitting supplemental or follow-up reports as required by 21 CFR 803.56.

The adequacy of your firm's response cannot be determined at this time. Your firm did not provide a revised MDR Procedure for review.

2. Failure to implement MDR procedure, as required by 21 CFR 803.17(b)(1). For example, your firm's MDR procedure, MDR Medical Device Reporting/ Vigilance, G-A-851-P-2, revision 2, Issued on July 26, 2013, describes a process for documentation and recordkeeping that includesdocumenting deliberations and decision-making processes used to determine if a device-related death, serious injury, or malfunction was or was not reportable. However, your firm failed to document such information in Case #s **(b)(4)**, **(b)(4)** and **(b)(4)**.

Additionally, your firm's MDR procedure includes references to baseline reporting and annual certification, which are no longer required. We recommend that all references to Baseline Reports and Annual Certification be removed from your firm's MDR procedure (see: 73 Federal Register Notice 53686, dated September 17, 2008; and Fourth Notice, Federal Register, dated March 20, 1997: Medical Device Reporting, Annual Certification, Final Rule, respectively).

If your firm wishes to submit MDR reports via electronic submission it can follow the directions stated at the following URL:

http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm[1]

If your firm wishes to discuss MDR reportability criteria or to schedule further communications, it may contact the Reportability Review Team by email at ReportabilityReviewTeam@fda.hhs.gov

Additionally, we have determined that your firm's devices are not pre-amendment devices that were legally on the market in the United States prior to May 28, 1976. Your firm has not submitted adequate documentation that established that these devices are pre-amendment and thus "grandfathered" from the 510(k) and PMA requirements. In order for your firm to legally market these devices in the United States, your firm needs to take immediate action to submit 510(k) applications for those devices requiring them and bring the devices into full compliance with all applicable FDA laws and regulations. Since continued introduction into commerce of these devices causes them to be misbranded and adulterated, your firm should contact the Division of Premarket and Labeling Compliance, Office of Compliance, Center for Devices and Radiological Health to discuss your corrective action plan and the time line for submission of the required 510(k) application. The devices affected by this decision are:

- Uterine tenaculum hook
- Uterine tenaculum forceps
- Obstetrical forceps
- Gynecological forceps
- Circumcision clamps
- Endometrium
- Biopsy suction curette
- Vaginal dilator
- Uterine cannula
- Hemorrhoid ligator
- Urethral dilator
- Vascular clamps
- Vascular dilators
- Vascular tennelers
- Catheter cannula
- Thoracic trocar
- Valvulatome
- traction tongs
- Clamping Device with Ball and Socket for (Item# VM NL150)
- Hudson Burr, 0 12mm, 8 teeth, tapered (Item# VM NL180)
- Adson Perforating Bur, 0 14mm (Item# VM NL190)
- McKenzie Perforating Twist Drill, 0 13mm (Item# VM NL200)
- Hudson Burr 0 14mm, (Item# VM NL250)
- McKenzie Enlarging Burr, 0 16mm (Item# VM NL270)
- Braun Uterine Tenaculum Forceps (Item# VM GL850)

A follow up inspection will be required to assure that corrections and/or corrective actions are adequate.

Please notify this office in writing within fifteen business days from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, including an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again. Include documentation of the corrections and/or corrective actions (which must address systemic problems) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Please provide a translation of documentation not in English to facilitate our review.

Your firm's response should be sent to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Field Operations Branch, White Oak Building 66, Rm 2622, 10903 New Hampshire Ave., Silver Spring, MD 20993. Refer to CMS case#415984 when replying. If you have any questions about the contents of this letter, please contact: Daniel Walter, Chief, Foreign Enforcement Branch at 301-796-5587.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality management systems. Your firm should

investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring the products into compliance.

Sincerely yours,
/S/
Steven D. Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

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Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Links on this page:

1. http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm