U.S. Food and Drug Administration



# Inspections, Compliance, Enforcement, and Criminal Investigations

## Optovue Inc. 6/11/0

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
1431 Harbor Bay Parkway
Alameda. CA 94502-7070
Telephone: 510/337-6700

**WARNING LETTER**

VIA UPS EXPRESS AND FACSIMILE

June 11, 2010

Mr. Jay Wai
President
Optovile, Inc.
45331 Northport Loop W
Fremont, California 94538

Dear Mr. Wai:

During an inspection of your firm located in Fremont, California between December 8, 2009 and January 8, 2010, investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures the RTVue Optical Coherence Tomography (OCT) with the Normative Database (NDB). Based on the labeling of your product the RTVue OCT with NDB is indicated for the in vivo imaging and measurement of the retina, retinal nerve fiber layer, and optic disc as an aid in the diagnosis and management of retinal diseases.

Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321 (h), this product is a device because it is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

Our inspection revealed your device is adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. 351(f)(1)(B), because you do not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 2 U.S.C. 360e(a), or an approved application for an investigational device exemption (IDE) under section 520(g) of the Act, 21 U.S.C. 360j(g). The device is also misbranded under section 502(o) of the Act, 21 U.S.C. 352(o), because you did not notify the agency of your intent to introduce the device into commercial distribution, as required by section 510(k) of the Act, 21 U.S.C.360(k). For a device requiring premarket approval, under Title 21, Code of Federal Regulations (CFR) 807.81(b), the notification required by section 510(k) of the Act, 21 U.S.C. 360(k), is deemed satisfied when a PMA is pending before the agency. The kind of information you need to submit in order to obtain approval or clearance for your device is described on the internet at http://www.fda.gov/cdrh/devadvice/3122.html. The FDA will evaluate the information you submit and decide whether your product may be legally marketed.

Our inspection also revealed that your 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 any material or information respecting the device that is required to comply with the requirements under section 519 of the Act and 21 CFR Part 803 - Medical Device Reporting (MDR). Specifically, you have failed to establish written procedures for MDR as required by 21 CFR 803.17. For example, during a review of your firm's complaint handling process, it was revealed that you have not implemented procedures for handling MDRs because **(b)(4)** of **(b)(4)** employees responsible for the review of complaints have not received training to your MDR procedure.

The FDA acknowledges your voluntary action to correct software versions 3.5 and higher that have been distributed to customer by issuing a "Roll Back" software update. This software update is designed to remove the NDB feature and bring your device into compliance. In addition, we acknowledge the receipt of your responses to the list of FDA-483 observations and that you have promised to correct those observations. At this time, your corrective actions are on

going and the adequacies of them cannot be fully reviewed and evaluated.

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within 15 working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, which may include notification of your current and past customers. Your response should also include an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Additionally in your response, please indicate what you plan to do with existing stock and products in the field that have been previously shipped.

In addition, FDA noted nonconformance with regards to section 501(h) of the Act, 21 U.S.C. 351(h), due to deficiencies of the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at 21 C.F.R. Part at 21 C.F.R. Part 820. These deviations include, but are not limited to, the following:

1. Failure to validate the device software for the RTVue OCT with NDB, software versions 3.5 and 4.0 as required by 21 CFR 820.30(g). Specifically:

   a. Software 3.5 Version C, was tested between **(b)(4)**. The test result shows a failure with sequence **(b)(4)**. The failure was identified as **(b)(4)**, unreasonable video baseline, known "bug".

   b. Verification and Validation for Version D was approved on **(b)(4)** to address the test result identified from the testing of software Version C. Verification and Validation testing was performed on software 3.5 Version D, on **(b)(4)**. The report identifies a "Remaining Defect List" and Number **(b)(4)** is identified as "Critical", "Spectrometer Motor Error!" This software version was released on **(b)(4)** without addressing defect number **(b)(4)** and without supporting documentation software defect number **(b)(4)** was corrected.

   c. Verification and Validation test results/raw data for software 4.0, Version B, were performed on **(b)(4)** and **(b)(4)**. Sections of the test data were not performed, unsigned, and/or missing as follows:

      I. Section 16 - Cornea Module, not performed.
      II. Section 11 - Gridline Examine and Analyze, not performed.
      III. Section 10.2 - Verify **(b)(4)** new function, unsigned and undated.
      IV. Section 15 - Combined Progression of **(b)(4)** and **(b)(4)** scans, a test sequence was not performed.
      V. Unidentified Section, raw test data missing. This test section is signed-off by an employee, with a completion date of **(b)(4).**

d. Electronic sign-off copy of the Verification and Validation Report for software 4.0, Version B. found the following:

      I. Section 16 - all sequence is entered as pass without supporting data to demonstrate the test was performed
      II. Section 11 - all sequence entered as pass without supporting data to demonstrate the test was performed.
      III. Section 10.2 - contains an electronic signature of an employee, dated **(b)(4)**
      IV. Section 15 - all sequence entered as pass without supporting data to demonstrate the test was performed.
      V. Section 3.1 - Verify Calibration Data is entered as being completed on **(b)(4)** There is no supporting data t demonstrate sequence testing was performed. However, the last sequence test page of this test section is identical to a test performed by an employee on **(b)(4)**, not **(b)(4)** as entered into the firm's electronic sign-off copy.

   e. Verification and Validation report for software version 2.0 is not available for review. According to your employee, once the results are entered into your electronic report, the raw tests data are discarded. Therefore, you have no evidence the sequence testing was performed.

2. Failure to establish procedures for verifying that design outputs meets design input requirements as required by 21 CFR 820.30(f). Specially, design input criteria were established by the firm in the development of your clinical study to develop the NDB. The design output is to create a database that represents the normal population in all regions across the world. Once developed, the NDB allows clinicians to compare individual patient results to values observed in normal patient population. To create this database, specific inclusion and exclusion criteria were outlined for a multi-site study in the **(b)(4)**

   In the review of the data, it was identified that:

   a. A subject was enrolled into the study that met the exclusion criteria, but data obtained from this subject was included in the NDB.
   b. Clinical data collected from study subjects meeting the inclusion criteria were not including in the NDB.
   c. Data obtained and inputted into the NDB to represent the Hispanic population were all taken from the **(b)(4)** area, not from its multi-site locations.

3. Failure to implement compliant handling procedures in reviewing and evaluating customer reports of device failures as required by 21 CFR 820.198(a). Specially, in-house servicing records contain events of reported device failures that were not entered and/or handled as product complaints.

a. An electronic file titled, **(b)(4)** revealed service dates ranging from **(b)(4)**. This spreadsheet identify the date of service, unit model, serial number, consumer contact information, subject matter, the fix, the service date, an close date. In the review of the electronic record, the types of problems entered are as follows:

I. Cannot tum on SLD, RTVue 100 with software version 3.5.2.5. The correction was not identified and the source of the problem is identified as the scanner.
II. Segmentation failed on NHH4, RTVue 100 with software version 3.5.25. The correction is identified as "application" and the source of the problem was identified as "algorithm error".
III. Error, spectrometer signal auto, RTVue 100 with software 3.6.12. The correct is identified as "other" and the source of the problem is "other".
IV. Spectrometer failed, RTVue 100 with software version 3.5.2.5. The correction is identified a "part replacement" and the source of the problem is the spectrometer.
V. Spectrometer failed, RTVue 100 with software version 3.6.0.12. The correction is identified as "part replacement" and the source of the problem is the spectrometer.

b. An electronic file titled, "**(b)(4)** " contains a list of service call and/or complaints reported between **(b)(4)** and **(b)(4)**. The types of service issues and/or complaints found are as follows:

I. Found frame grabber bad, replaced frame grabber now appears spectrometer has other problems. The complaint closed without further investigation.
II. Customer is asking for assistance with video problem. Assisted with troubleshooting video problem, service closed without investigation.
III. Customer reported, unable to scan due to low signal strength. Your service representative went online and discovered the spectrometer signal almost flat with thick red line. Service representative was unable to reduce noise or raise signal strength, and noted the spectrometer requires replacement. Case closed without further investigation.
IV. Customer having problems with spectrometer and has been replaced twice. Recommend replacing scanner and CAM, rev. B. Scanner to be shipped. Case closed without further investigation.

c. An electronic file titled "**(b)(4)**", containing a list of service issues from **(b)(4)**. The types of service Issues found include:

I. Customer received an error message: "Spectrometer motor not exist or too slow". The problem was identified as the spectrometer's stepper motor requiring replacement. The part was shipped to customer and problem resolved. Case closed without performing an investigation.
II. Customer called and reported low signal readings on their scans. Firm verified bold red signal on the spectrometer readings. The scanner was repaired and the case closed without performing an investigation.
III. Customer report continuous problem with the spectrometer signal, "Unable to initialize spectrometer auto alignment". Your service technician cannot trouble shoot the problem. The reported event was corrected by rebooting and the case closed without performing an investigation.
IV. Customer report SLD and PZT alignment error. Adjustments were made to the device and reported to wor properly. Customer called again and reported field service visited site, made adjustments to machine, and the original error message returned. The problem was corrected by replacing a scanner part. Case closed without performing an investigation.

d. The review of clinical study reports shows reported failures that were not investigated. In the review of clinical study reports, there were many reports of weak signals and abnormal VF. These reported device failures were no investigated or identified as consumer complaints.

e. The review of marketing questionnaires shows reported events where the device did not perform as expected. No reports were generated to evaluate or investigate the noted problems of product dissatisfaction.

4. Failure to establish procedures to ensure that all complaints are evaluated to determine whether a complaint should be filed as a Medical Device Report as required by 21 CFR 820.198(a)(3). Specially, your complaint procedure lacks the ability to capture patient involvement; therefore, you are unable to evaluate whether the complaint represents an event requiring the submission of a Medical Device Report as required by 21 CFR 820.198(a)(3).

5. Failure to establish Servicing procedures as required by 21 CFR 820.00(a). Specially, your service manual does no address issues related to software failures.

6. Failure to ensure employees are adequately trained to perform their assigned duties as required by 21 CFR 820.25(b). Specially, you have **(b)(4)** Technical Support Engineers. As outlined by the position description, these individuals are responsible for providing verbal and written support to end users, sales representatives, and international distributors. These individuals are also responsible for resolving service and technical problems. In the review of training records, **(b)(4)** employees received training to the firm's complaint handling and MDR procedures. Additionally, your training procedure, DOC# **(b)(4)**, date **(b)(4)** shows that each department manager/supervisor is responsible for ensuring that all their employees, contractors, and consultants are qualified and trained to perform their assigned job and to ensure that there are records of formal training. Additionally, during a Technical Support Personnel do not have the necessary education, background, or experience to adequately

perform their job duties. According to "**(b)(4)**", it states that technical support personnel are responsible for decidin "Case Reason" and determining if the "Report received that reasonably suggest one of Optovue's marketed devices may have caused or contributed to death or serious injury of a patient," or "Report received that reasonably suggest a device malfunction(s) has the potential to cause serious injury, serious unanticipated deterioration in health or death of a patient, user or other person." A review of **(b)(4)** technical support personnel's resumes shows that **(b)(4)** individuals have training, education, and experience in the fields of electronic specific to installation, upgrading, and repairing and maintenance of equipment. Neither individual has any medical background or experience in order to determine if"a device malfunction(s) has the potential to cause serious injury, serious unanticipated deterioration in health or death of a patient, user or other person."

Your response should be sent to: Mr. Lawton Lum, Compliance Officer, 1431 Harbor Bay Parkway, Alameda, California 94052. If you have any questions about the content of this letter please contact: Mr. Lum at (510) 337-6792 or by fax at (510) 337-6703.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your facility. is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Sincerely yours,

/s/

Barbara J. Cassens.
District Director

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