U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Hoya Corporation 8/12/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
White Oak Building 66
Silver Spring, MD 20993

WARNING LETTER
AUG 12, 2015

VIA UNITED PARCEL SERVICE

Mr. Hiroshi Suzuki
President and CEO
Hoya Corporation (PENTAX Life Care Division)
Showanomori Technology Center
1-1-110 Tsutsujigaoka, Akishima-shi
Tokyo 196-0012
Japan

Dear Mr. Suzuki:

The United States Food and Drug Administration (FDA) conducted the following inspections at your facilities:

- Hoya Corporation (PENTAX Life Care Division) located at 1-1-110 Tsutsujigaoka, Akishima-shi, Tokyo 196-0012, Japan, on April 13, 2015 through April 21, 2015;

- Hoya Corporation (PENTAX Life Care Division), Miyagi Factory, located at 30-2 Okada, Aza-Shimomiyano, Tsukidate, Kurihara-shi, Miyagi, 987-2203, Japan, on April 22, 2015 through April 24, 2015; and
- Pentax of America, Inc., located at 3 Paragon Drive, Montvale, New Jersey 07645-1725, on March 31, 2015 through April 2, 2015.

During these inspections investigators from the FDA determined that your firm manufactures endoscopes and endoscope accessories. 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 are intended to affect the structure or function of the body.

These inspections revealed that your firm's 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 (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received responses from Mr. Tomokazu Kishi, Senior General Manager, and Wijnand Stijn, Global Vice President of Quality Assurance and Regulatory Affairs, dated May 12, 2015, May 15, 2015, and June 30, 2015, concerning our investigators' observations noted on the Form FDA 483s (FDA 483), List of Inspectional Observations, that were issued to your firm. We address these responses below, in relation to each of the noted violations. 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, failure to include testing of production units under actual or simulated use conditions, and failure to document the results of the design validation in the device history file (DHF), as required by 21 CFR 820.30(g). For example:

a. The validation studies conducted to support the Ethylene Oxide (EtO) sterilization and cleaning and high level disinfection (HLD) Instructions for Use (IFUs) for the currently marketed device, ED-3670TK, were conducted using different model/series endoscopes. Your firm failed to document why design validation results for the different model/series endoscopes are valid and applicable to the ED-3670TK devices [Akishima-shi, Tokyo].

b. Labeling document **(b)(4)**, Revision A, states that an EtO/Carbon Dioxide (80:20 gas mixture) and EtO/Carbon Dioxide (90:10 gas mixture) can be used to sterilize endoscopes. However, your firm did not use the specified gas concentrations for validation. The validation for the ED-3490TK and ED-3670TK devices was conducted with EtO/HCFC (Oxyfume 2001) (10:90 gas mixture) [Akishima-shi, Tokyo].

c. Your firm failed to document in the DHF the protocol and the raw data associated with:

i. The final EtO sterilization validation report, **(b)(4)**, laboratory number **(b)(4)**, for the ED-3490TK and ED-3670TK devices [Akishima-shi, Tokyo].

ii. The protocol and the raw data associated with the HLD validation report **(b)(4)** were not documented in the DHF [Akishima-shi, Tokyo].

d. Validation protocol no. **(b)(4)**, used to support the reprocessing of the ED-3490TK and the ED-3670TK devices, does not specify the validation testing conditions. For example, the cleaning protocol requires using a syringe filled with an enzymatic detergent to flush the suction channel. However, the volume of the syringe and the type of detergent are not specified [Akishima-shi, Tokyo].

We reviewed your firm's responses and conclude that they are not adequate. Your firm initiated corrective and preventive action (CAPA) to address the above design validation deficiencies. However, your responses indicated that these CAPAs have not been completed. Your firm also has not retrospectively reviewed other design validations to ensure that they are adequate.

2. Failure to establish and maintain procedures for verifying the device design to confirm that the design output meets the design input requirements and failure to document in the the results of the design verification as required by 21 CFR 820.30(f). For example, your firm does not have documentation to demonstrate that criteria for the design verification were met for the ED-3490TK devices [Akishima-shi, Tokyo).

We reviewed your firm’s responses and conclude that they are not adequate. Your firm initiated a CAPA to address the above design verification deficiency for duodenoscopes. However, your firm's responses indicated that this CAPA has not been completed. Your firm also has not retrospectively reviewed other design verifications to ensure that they are adequate.

3. 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 received complaints regarding foreign objects lodged in the channel of duodenoscopes after manual cleaning and reprocessing, as observed by the user. Your firm filed three MDRs associated with fragments of cleaning brushes, stents, and a dilation balloon found lodged in the channel of the duodenoscopes, and initiated CAPA 000004. As part of the corrective actions, your firm updated its Risk Management. File to indicate that the cleaning/disinfection efficacy cannot be achieved due to the obstruction, and identified this hazard as "critical.” Your firm subsequently implemented the use of a ball probe inspection tool on scopes received for repair or servicing.

However, your firm's corrective actions did not address how mechanical obstructions should be handled by the user. The foreign objects lodged in the channel of duodenoscopes can become dislodged inside the patient, if not removed during manual cleaning. Your firm failed to evaluate whether the indications for use (IFUs) need to be updated to include safety statements regarding how users should handle mechanical obstructions. Also, your firm did not evaluate whether the ball probe inspection tool should be provided to the end users [Akishima-shi, Tokyo].

b. CAPA QS-13-006 identified corrective actions to your firm's software validation procedure and identified 50 software processes that were not validated. Your firm closed the CAPA as effective on April 15, 2015; however, the validations for 38 of the identified software processes were not completed [Kurihara-shi, Miyagi].

The adequacy of your firm's responses cannot be determined at this time. Your firm initiated a CAPA to address the above deficiencies. However, your firm has not completed implementation of its corrective actions and CAPA effectiveness verifications for this observation.

4. Failure to ensure that when the results of a process cannot be fully verified by subsequent inspection and test that the process shall be validated with a high degree of assurance and approved according to established procedures, as required by 21 CFR 820.75(a). For example, the tip water leakage test method used in the manufacture/inspection of the ED- 3490TK devices has not been validated. The tip water leakage test is an in-process test conducted after the elevator cover has been sealed to the distal body [Kurihara-shi, Miyagij.

We have reviewed your firm's responses and conclude that they are not adequate. Your firm initiated a CAPA to address the above process control deficiency. However, your firm's responses indicated that this CAPA has not been completed. Additionally, your firm has not retrospectively reviewed other manufacturing processes to ensure that they are adequately validated.

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 (MDR). Significant violations include, but are not limited to, the following:

5. Failure to report to FDA no later than 30 calendar days after the day that Hoya Corporation received or otherwise became aware of information, from any source, that reasonably suggests that a device that your firm markets may have caused or contributed to a death or serious injury, as required by 21 CFR 803.50(a)(1). For example, Hoya Corporation, Akishima-shi, Tokyo, Japan, facility failed to submit initial Medical Device Reports (MDRs) for each patient who developed a *Carbapenem Resistance Enterobacteriaceae* infection after an endoscopic procedure involving your firm's duodenoscopes. This information was reported by your firm's importer, PAI, in MDRs#2518897-2013-00004, #2518897-2013-00005, and #2518897-2013-00006, and the associated supplemental reports. In addition, your firm failed to submit initial MDRs for each of the seven events referenced in MDR #2518897-2014-00001 and for each of the two events referenced in MDR #2518897-2014-00002 [Akishima-shi, Tokyo].

6. Failure to adequately develop, maintain and implement written MDR procedures, as required by 21 CPR 803.17. For example after reviewing your firm's MDR procedure, Medical Device Reporting, WI #402-007, Effective Date: November 1, 2013, Revision A, the following issues were noted:

a. The procedure does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements [Montvale, New Jersey]. For example:

> i. The procedure fails to describe the process that other Pentax Medical regions, including firms outside the U.S., will follow to ensure that Pentax of America receives all necessary information that will allow Pentax of America to submit all required information on the Mandatory 3500A report form for all parties.

ii. Section 5, "Implementation," states that "an event is considered reportable when PENTAX of America has received or otherwise become aware of information that reasonably suggests..." Please note that when submitting MDR reportable events to FDA on behalf of other Pentax regions, including the firms outside the U.S., the MDR should be submitted within 30 calendar days after the day that each specified region becomes aware of a reportable death, serious injury, or malfunction, as required by 21 CFR 803.10(c)(1).

b. The procedure does not establish internal systems that provide for timely transmission of complete medical device reports. Specifically, your firm did not address the circumstances under which Pentax of America must submit supplemental or follow-up reports on behalf of the manufacturer and the requirements for such reports [Montvale, New Jersey].

c. Your firm's MDR procedure does not describe the process that Hoya Corporation will follow to submit MDRs to FDA, if it becomes aware of an MDR reportable event. As a device manufacturer, Hoya Corporation is responsible for submitting MDRs to FDA in accordance with the requirements in 21 CFR 803.50(a) and 21 CFR Part 803.52 [Akishima-shi, Tokyo].

d. PENTAX of America, Inc. (PAI), meets the definition of an importer in 21 CFR 803.3, and is subject to the reporting requirements found in 21 CFR 803.40 and 21 CFR 803.42. Hoya Corporation should submit a request for an exemption to cover the reporting agreement with PAI. Please be advised that Hoya Corporation is responsible for submitting initial MDRs to the FDA until an exemption is granted [Akishima-shi, Tokyo, and Montvale, New Jersey].

For information regarding exemption requests, please contact the MDR Policy Branch at: **MDRPolicy@fda.hhs.gov (/MedicalDevices/default.htm)**.

The eMDR Final Rule requiring manufacturers and importers to submit electronic Medical Device Reports (eMDRs) to FDA was published on February 13, 2014. The requirements of this final rule will take effect on August 14, 2015. If your firm is not currently submitting reports electronically, we encourage you to visit the following web link for additional information about the electronic reporting requirements:

http://www.fda.gov/ForIndustry/FDAeSubmitter/ucm107903.htm (/default.htm)

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 (/default.htm)**

U.S. federal agencies may be advised of the issuance of 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.

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 Inspections Support Branch, White Oak Building 66, Rm 2622, 10903 New Hampshire Ave., Silver Spring, MD 20993. Refer to CMS case #461447 when replying. If you have any questions about the contents of this letter, please contact: Daniel Walter, Chief, Foreign Enforcement Branch at +1 (301) 796-5587, or fax +1 (301) 847-8139.

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/
Jan B. Welch, MHS, MT (ASCP) SBB
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

And

/S/
Diana Amador-Toro
District Director
New Jersey District

cc: Mr. Ganesh Ramaswamy
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