



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

1120791

SEP 30 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER WITH DENTENTION WITHOUT PHYSICAL EXAMINATION
VIA FEDERAL EXPRESS

Dr. Guiseppe Ammendola
President and Managing Director
Villa Sistemi Medicali, S.p.A.
Via delle Azelae 3
20090 Bucinasco (Milan)
ITALY

Dear Dr. Ammendola:

During an inspection of your firm located in Bucinasco (Milan), Italy, on May 11-15 & 18, 1998, our Investigator determined that your firm manufactures the Aztech 65, dental X-ray Systems. This product is a device as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (The Act).

The above-stated inspection revealed that this device is adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for its manufacture, packing, storage, or installation is not in conformance with the current good manufacturing practice (CGMP) requirements of the Quality System Regulation, as specified in Title 21, Code of Federal Regulations, (CFR), Part 820. The 1978 Good Manufacturing Practices (GMP) was superseded on June 1, 1997, by the Quality System Regulation.

1. Failure to establish adequate procedures for receiving, reviewing and evaluating complaints as required by 21 CFR 820.198(1), (2) & (3). For example, complaint procedures do not assure that:
 - (a) all complaints are handled in a uniform and timely manner;
 - (b) all written and oral complaints are documented upon receipt and;
 - (c) all complaints are reviewed for MDR applicability and investigation.

Your response is not adequate. Your response provides a revised copy of the "Complaint Handling Procedure, VSM # [redacted]", Rev. [redacted], dated 7/1/98, (written in Italian). Your response explains that this revised procedure will correct the deficiencies. Please provide an English translation.

2. Failure to establish and maintain procedures for implementing corrective and preventive action which includes analyzing processes to identify existing and potential causes of non-conforming product, and investigating the causes of non-conformities relating to product or other quality problems as required by 21 CFR 820.100(a)(1). For example:

- (a) There are no formal procedures to control and define the collection and analysis of failure data. Some data is collected currently, but not for U.S. products.
- (b) The failure investigation procedures do not assure the return of failed product/component for investigation.

Your response is not adequate. Your response provides a copy of the new "Failure Investigation Procedure, VSM # [REDACTED]", dated 6/29/98, (written in Italian) and "Failure Investigation [REDACTED]", Rev. 0, dated 6/29/98, an unsigned English translation. This procedure references 21 CFR 820.162, Failure Investigation that is covered by the former GMP requirement. The procedure provided does not adequately address the Quality System Regulation requirements.

3. Failure to follow written final acceptance activities procedure to assure that device specifications are met and that the release of the finished devices is authorized by the signature of a designated individual as required by 21 CFR 820.80(d)(1) and (3). For example, final test records were signed by a non-Villa employee when only part of the testing was done. The final test record was not signed as approved by Villa Sistemi Medicali.

Your response is not adequate. Your response states that the final test records will be signed and approved by VSM employees and that suppliers have been instructed in the new requirement. No document was provided that indicated what instructions were given to the supplier. A copy of the Timer Test Procedure, CCD Timer, [REDACTED], Rev. 2, dated 6/28/98, was provided (written in Italian). A copy of the Timer Test Procedure, CCD Timer, [REDACTED], Rev. 3, and Test Report not filled-out (written in English) both dated 7/24/98, were provided as preliminary copies. The Timer Test Procedure does allow for a QA signature, but no date is required.

4. Failure to ensure that a finished device is not released for distribution until: (1) the activities required by the device master record are completed; (2) the associated data and documentation is reviewed; (3) the release is authorized by the signature of a designated individual(s) and (4) the authorization is dated as required by 21 CFR 820.80(d). For example, test records lack required test results and/or showed out of specification results without indication of recognition of QA.

Your response may be adequate. Your response provides the revised "Tube Head Assembly Procedure, VSM [REDACTED], Rev. 3, dated 6/29/98, (written in Italian and English. You indicate in your response that all units present at VSM were retested using the revised procedure. However, you only provided (3) three records from a lot of 50 units, which were based upon, the new revised [REDACTED], Rev.3. Additionally, your consultant provided a preliminary copy of "Aztech 65 Test Procedure, No. [REDACTED]", Rev. 4, dated 7/24/98, (written in English) which does require QA involvement. Please provide us with the most current Tube Head Assembly Procedure, along with documentation, which provides evidence of implementation.

5. Failure to establish and maintain procedures for acceptance activities, which includes inspections, tests, or other verification activities as required by 21 CFR 820.80. For example, some timer control sheets lack required QA approval.

Your response is not adequate. The new timer test procedure noted in item 3 above requires that a Quality Control Supervisor provide a final signature for the timer Test report but no date is required.

6. Failure to follow receiving acceptance procedures to assure that incoming product meet specified requirements as required by 21 CFR 820.80(b). For example, a lot of x-ray tubes were accepted without evidence of a required certificate from the manufacturer.

Your response is adequate.

7. Failure of the in-process acceptance procedures to assure that in-process product is controlled until the necessary approvals are received and documented as required by 21 CFR 820.80(c). For example, a review of the procedures and production records for the Tubehead

assembly revealed that there is no evidence of QA involvement or approval.

Your response is not adequate. Your response states that the new "Device History Record Procedure, VSM # [REDACTED]", dated 6/26/98, (written in Italian), allows for QA involvement. Your response further states that QA will review the completed DHR for completeness and correctness. Please provide an English translation of the Device History Record Procedure and evidence of implementation.

8. Failure to maintain Device Master Records (DMR) that includes or refers to the location of: device specifications including component specifications, software specifications; production process specifications; quality assurance procedures; and labeling specifications as required by 21 CFR 820.181 (a), (b), (c) and (d). For example, the firm has no Device Master Record for the Aztech 65.

Your response is not adequate. Your response provides "Device Master Record Procedure VSM # [REDACTED]", dated 6/29/98, (written in Italian), that you indicate includes or refers to all the elements of the DMR. Also, included was a copy of Device Master Record, DMR # [REDACTED], dated 6/30/98, also written in Italian. Additionally, an English translation of the T526, Aztech 65 Tube Head Assembly and collimator, Test Procedure, Rev.3, dated 6/29/98, and a preliminary copy of the procedure, [REDACTED], Rev. 4, dated 7/24/98, was submitted by your consultant. Further, your response provides an English translation of Time Test Procedure, [REDACTED], Rev. 2, dated 6/28/98, and your consultant provided a preliminary copy of this Time Test Procedure, [REDACTED], Rev. 3, dated 7/24/98. These procedures were the only translated documents provided by you. The remainder of the DMR procedures were written in Italian. Please provide an English translation of the remaining DMR documents.

9. Failure to establish and maintain Device Master Records (DMR) that include, or refer to the location of component specifications and quality assurance procedures and specifications as required by 21 CFR 820.181. For example, a review of the device history record inspections files for incoming components revealed that there are no specification sheets or inspection steps for the Aztech X-ray scissor-arms and extender arms.

Your response is not adequate. Your response provides a copy of your new "Failure Investigation Procedure, VSM # [REDACTED], dated 6/29/98, (written in Italian) and

"Failure Investigation, [REDACTED], Rev.0, dated 6/29/98, an English translation, that was submitted by your consultant. This procedure is based upon 21 CFR 820.162, Failure Investigation, which was covered by the former GMP requirement. This procedure does not adequately address the Quality System Regulation (QS) requirements.

10. Failure to maintain Device History Records (DHR) that include the quantity manufactured; acceptance records which demonstrate that the device is manufactured in accordance with the DMR and primary identification label required by 21 CFR 820.184(b), (d) and (e). For example, there is no Device History Record for the Aztech 65 that contains or refers to acceptance records, primary identification label, and quantity manufactured.

Your response is not adequate. Your response provides the "Device History Record Procedure VSM # [REDACTED], " dated 6/26/98, (written in Italian) and approved DHR Form, Mod. [REDACTED], dated 6/26/98. Additionally, you submitted a copy of a Device History Record dated 7/6/98, which indicated the retesting of three (3) Aztech 65 units from a 50 unit lot. Your response included copies of Packaging lists, Rev. 1, dated 2/14/98, Mod. [REDACTED], for the 3 Aztech 65 units shipped without Quality Assurance approval. Please give a rationale why only three (3) records were provided out of a shipment of 50 units. The labels you provided are not readable due to xeroxing/photocopying and some are filled-in while others are not filled-in. There is no clarity and/or explanation of these labels. Most of the documents submitted are written in Italian. Please provide an English translation of the device history record procedure and clarify/explain the labeling that you provided.

11. Failure of the device history record to demonstrate that each batch, lot, or unit is manufactured in accordance with the device Master record as required by 21 CFR 820.184. For example:
 - (a) Exposure times were outside exposure time accuracy specifications and were not corrected.

- (b) Exposure was possible outside the +/- voltage range, but was not corrected or addressed by production or QA.

Your response is not adequate. Your response indicates that the retesting of units at VSM has determined that all units are within specification range. The (3) test records mentioned previously in item 10 above still indicates that you are still recording voltage variance/emission test results outside the 120v +/- specification ranges. Additionally, your response states that previous units were within specification range but that they were recorded incorrectly. Regarding the exposure times outside of the +/- voltage range, your response provides "Timer Test Procedure Aztech 65, Kono 70, VSM no. and the test record form Rev. 2, dated 6/28/98, (written in Italian) and Rev. 3, a preliminary copy dated 7/ 24/98 (written English) as previously mentioned. This procedure specifies a measurement tolerance for the exact test voltages for which x-ray emission must occur and when emission must not occur. However, you did not provide any documentation that indicates whether the new acceptance specifications had been validated or when through a design control review/process. Additionally, your response does not give any indication whether these new changes will be submitted in a supplement to the initial report.

12. Failure of the device history record to demonstrate that the device is manufactured in accordance with the device master record as required by 21 CFR 820.184. For example, the processing log for autoclaving/oil filling lacked required data.

Your response is not adequate. You did not address this deficiency in your response.

13. Failure of the device history record, acceptance record, to demonstrate that the device is manufactured in accordance with the Device Master record as required by 21 CFR 820.184(d). For example, there is acceptance of a reworked component without inspection or review to assure the adequacy of the rework.

Your response is not adequate. Your response provides a copy of your new "Failure Investigation Procedure, VSM #", dated 6/29/98, (written in Italian) and "Failure Investigation", Rev. 0, dated 6/29/98, a unsigned English translation submitted by the your consultant. The procedure is based upon 21 CFR 820.162, Failure Investigation, which is covered by the

former GMP requirement. The procedure provided does not adequately address the Quality System Regulation requirements.

14. Failure to implement procedures that address identification, documentation, evaluation, segregation and disposition of nonconforming product; and establish and maintain procedures for rework to include retesting and reevaluation of the nonconforming product as required by 21 CFR 820.90(a) and (b)(2). For example:

- (a) In process failures of timer pcbs are not recorded or tracked.
- (b) The THAs that failed during testing were lined out the test record and reportedly reworked. There is no documentation or Non-Conformity Form (NCF) filled out to show what was done and the status of the THA.

Your response is not adequate. Your response provides a copy of your new "Failure Investigation Procedure, VSM # [REDACTED]", dated 6/29/98 (written in Italian) and "Failure Investigation [REDACTED]", Rev. 0, dated 6/29/98, a unsigned English translation. The procedure is based upon 21 CFR 820.162, Failure Investigation covered by the former GMP requirement and does not adequately address the Quality System Regulation requirements. Also, included with this procedure is a nonconformance form, Nr [REDACTED] that was not filled-out.

15. Failure to establish a sampling plan based on a valid statistical rationale as required by 21 CFR 820.250(b). For example, the incoming inspection of timers revealed the use of the incorrect sampling plan (reduced instead of tightened sampling).

Your response is not adequate. Your response provides "Sampling Procedure VSM # [REDACTED] dated 6/27/98 (written Italian). You indicate that this sampling procedure is based upon ISO [REDACTED] sampling. Your response states that your personnel will be retrained in the use of the new procedure. However, you did not give any indication when this training would occur. You also state that that during an audit by Quality Assurance they would verify the corrective action taken. No date for the audit was given. A letter from your consultant indicates that timers are already [REDACTED] tested. However, no documentation was provided to confirm [REDACTED] testing of the timers. Please provide a translation of the sampling procedure; documentation of training if it has occurred or give date of intention;

the date of the audit by quality assurance and; evidence of 100% timer testing.

16. Failure to ensure that sampling plans used are adequate for their intended use and to ensure that when changes occur the sampling plans are reviewed and documented as required by 21 CFR 820.250(b). For example, there is no formal documentation to show the review and approval/authorization, and effectivity date of the following significant changes in processes and procedures:

- (a) changes in sampling plan AQL;
- (b) the establishment of a general AQL of [REDACTED] for components without any documented rationale behind selecting this particular level/AQL and;
- (c) the establishment of a [REDACTED] sampling plan for some tests;

Your response is not adequate. Your response provides "Sampling Procedure VSM # [REDACTED] as noted in item 15 above (written Italian). Your response indicates that all subsequent changes for the sampling plan and assembly test procedures will be approved in accordance with your document control procedures. No document control procedure was provided. Additionally, your consultant letter states that your firm proposes to return to [REDACTED] testing for all tubehead assembly tests. Please provide an English translation of the sampling procedure and a copy of your document control procedures.

17. Failure to establish adequate procedures for identifying product during all stages of production to prevent mix-ups as required by 21 CFR 820.60. For example, rejected components were not identified with the required "do not use" stickers.

Your response is not adequate. Your response provides a copy of the new "Failure Investigation Procedure VSM # [REDACTED], dated 6/29/98, (written in Italian) and a unsigned English translation as previously noted in item 14 above. This procedure is based upon 21 CFR 820.162, Failure Investigation covered by the former GMP requirement and does not adequately address the Quality System Regulation requirements. However, this procedure does address the clarification of the use of the [REDACTED] or [REDACTED] "do not use" stickers.

18. Failure to maintain records of changes to documents which includes a description of the change, identification of the affected documents, the signature of the approving individual(s), and when the change becomes effective as required by 21 CFR 820.40(b). For example, there is no formal documentation to show the review and approval/authorization, and effectivity date for the changes to tubehead assembly testing (impulse count, leakage).

Your response may be adequate. Your response provides a copy of "Procedura Di Collaudo, Aztech 65, Kono 70" Rev. [REDACTED], dated 4/30/98, (written in Italian). Your response states that you approved a change from revision [REDACTED] to revision [REDACTED] of the test procedure on 4/30/98. Please provide an English translation of Procedura Di Collaudo.

19. Failure to have changes made to documents reviewed and approved by an individual as required by 21 CFR 820.40(b). For example, there is no formal documentation to show the review and approval/authorization, for the release of the 4/6/98 revision of the Aztech 65 manuals and the following instances of formal documented changes without evidence of validation or verification:

- (1) RDM [REDACTED], dated 3/2/98, and accepted 3/20/98.
- (2) RDM [REDACTED], dated 3/3/98, and accepted 3/20/98.
- (3) RDM [REDACTED], dated 2/18/98, and accepted 5/7/98.
- (4) RDM [REDACTED], dated 1/23/98, and accepted 1/26/98.
- (5) RDM [REDACTED], dated, 11/14/97, and accepted 12/11/97.

Your response is not adequate. Your response states that the "Manual Control Procedure, VSM [REDACTED], dated 2/27/98, (written in Italian) was used to control the release of revision [REDACTED], Installation and User Manual (Aztech 65) on 4/6/98. Your response further states that you revised your "Change Control Procedure, VSM [REDACTED]", and that it will include the release of new manuals, however, no change control procedure document was provided. Please provide an English translation of the manual control procedure and a copy of your change control document.

20. Failure to evaluate and select suppliers on the basis of their ability to meet specified requirements, including quality requirement and document the evaluation as required by 21 CFR 820.50(a)(1). For example, there is no formal

documentation for the change of one printed circuit board manufacturer to another.

Your response is not adequate. Your response states that the new circuit board supplier was evaluated and a declaration of qualification was issued. You did not provide a copy of the declaration of qualification document. Additionally, your response indicates that you are revising "Purchasing Procedure Quality Manual Procedure # [REDACTED]," dated 3/3/98. A copy of this procedure was provided (written in Italian). Please provide a copy of the declaration of qualification and an English translated copy of your purchasing procedure.

21. Failure to establish and maintain procedures to ensure that equipment is routinely calibrated and maintained as required by 21 CFR 820.72(b). For example, there are no written calibration procedures for the reference timer used to verify CCD timer and kVp accuracy.

Your response is not adequate. Your response provides a copy of a document that indicates the calibration of the referenced timer was completed and current. However, you did not provide a calibration procedure. Please note that this deficiency was not included on the FDA 483, however, it was discussed by the investigator with you.

22. Failure to establish and maintain procedures for the control of storage areas and stockrooms for product to prevent damage or other adverse effects pending use as required by 21 CFR 820.150. For example, the printed circuit boards were stored in a manner conducive to damage and adverse effects.

Your response is not adequate. Your response provides two new procedures "ESD Control Procedure, VSM [REDACTED] and [REDACTED], Rev. [REDACTED], both dated 7/3/98, (written in Italian). Your response explains that these new procedures address Electrostatic Discharge (ESD) and physical handling requirements for printed circuit boards.

Additionally, the above stated inspection revealed that your firm was not in compliance with the Medical Device Reporting (MDR) requirements set forth under 21 CFR 803.17. Specifically, you failed to develop, maintain and implement written Medical Device Reports (MDR) procedures as required.

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Your response is not adequate. Your response provides "Incident Procedure, VSM # [REDACTED], Rev. 1, dated 7/1/98, (written in Italian). Your response explains that MDR requirements are addressed by this procedure. Please provide a English translation of the incident procedure.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations.

The specific violations noted in this letter and the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration (FDA). If the causes are determined to be systems problems, you must promptly initiate permanent correction actions. 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.

We acknowledge that Villa Sistemi Medicali, S.p.A., Buccinasco, (Milan), Italy has submitted to FDA, responses dated July 3, 1998 and August 6-7, 1998. Additionally, your consultant, [REDACTED], M.S, submitted responses dated July 24, 1998, July 28, 1998, and August 4, 1998. These responses were concerning our investigators' observations noted on the FDA 493 form. We have reviewed these responses and have concluded that they are inadequate as described above.

Given the serious nature of these violations of the Act, the Aztech 65, dental x-ray system, manufactured by Villa Sistemi, may be detained without physical examination upon entry into the United States (U.S.) until these violations are corrected. You should take prompt action to correct these deviations.

In order to remove the devices from this detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections has been verified, your products may resume entry into this country.

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Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken or intend to take to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. 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. Please include any and all documentation to show that adequate corrections have been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If documentation is not in English, please provide a translation to facilitate our review.

Please direct your written response to Ms. Fleadia R. Farrah of the Diagnostic Devices Branch, Division of Enforcement I at the above letterhead address. Should you require any assistance in understanding the contents of this letter, do not hesitate to contact her at this address, telephone (301) 594-4591 or telefax (301) 594-4636.

Sincerely yours

for Adrienne Galdi

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

cc:

[REDACTED]