



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Purged 10/20/97
Joseph J. Salyer
Public Health Service
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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER

VIA FEDERAL EXPRESS

Daud Mohamad, Ph.D.
Deputy Director General (Corporate)
Malaysian Institute for Nuclear Technology Research (MINT)
Bangi
43000 Kajang, Malaysia

Dear Dr. Mohamad:

During an inspection of your firm located in Kajang, Malaysia, on March 19-20, 1997, our Investigator determined that your firm irradiates medical devices, pharmaceuticals, foods, cosmetics and other products.

The above-stated inspection revealed that products irradiated at Sinagama, Bangi, Kajang, Malaysia, are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practices (GMP) regulations of 1978, as specified in Title 21, Code of Federal Regulations (CFR) Part 820. The 1978 GMP regulation was superseded on June 1, 1997, by the Current Good Manufacturing Practice (CGMP) requirements as set forth in the Quality System Regulation, 21 CFR Part 820. The deficiencies noted during the inspection reference the 1978 GMP requirements, with a cross reference to the new 1997 Quality System Regulation. We have not received a response from your firm regarding the observations noted in the FDA 483 by the Investigator.

1. Failure to establish and implement specification control measures to assure that the design basis for the device is correctly translated into approved specifications, as required by 21 CFR 820.100(a)(1). This would also be a violation of the Quality System Regulation, 21 CFR 820.75(a). For example:
 - a) There is no established protocol and rationale for the routine dosimeter placement at minimum and maximum locations. The routine placements are not consistent with the dose mapping by the primary, secondary, and internal laboratories.
 - b) There is no reason for validation or re-validation documented on the Dose Validation Reports.

- c) The written dose validation procedure does not stipulate the allowable [REDACTED] difference between the actual minimum/maximum dosage values obtained and the specified minimum/maximum dosage values for products.
 - d) The written dose validation procedure does not stipulate the allowable [REDACTED] difference between the routine minimum/maximum dosage values obtained and the currently established minimum/maximum dosage values for source/cycle.
 - e) Dose Validation Reports do not reference where dose location specifications were obtained for various minimum/maximum dosage values documented in the Operator Instructions.
 - f) There is no written schedule of dose validation for customers after source realignment or addition, to assure all customer's products are acceptable for the new minimum/maximum dose mapping of the irradiation cycle.
 - g) There is no tracking documentation for incoming products to assure that the product has been validated for the irradiation cycle being used. (This was not listed on the FDA-483, but was included in the Establishment Inspection Report by the Investigator.)
2. Failure to follow a formal approval procedure for any change in the manufacturing process of a device, as required by 21 CFR 820.100(b)(3). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(b). For example, there is no documentation explaining routine dosimeter location changes. (This was not listed on the FDA-483, but was included in the Establishment Inspection Report by the Investigator.)
 3. Failure of the device master record to include, or refer to the location of, any authorized changes in production process specifications, as required by 21 CFR 820.181. This would also be a violation of the Quality System Regulation, 21 CFR 820.181. For example, there is no master list with revisions, or reference to their archived location, where dosimeters are to be placed during the irradiation cycle.
 4. Failure of the device master record to include, or refer to the location of, quality assurance procedures and specifications including quality assurance checks used and the quality assurance apparatus used, as required by 21 CFR 820.181(c). This would also be a violation of the Quality

System Regulation, 21 CFR 820.181(c). For example, the written procedure for reading dosimeters does not include complete instructions for quality assurance personnel, such as:

- a) The expected value of non-irradiated solution, maintenance of the solution, and actions to be taken if the value is out of range are not included.
 - b) The temperature reading specification and location to be read are not included.
 - c) Precautions to protect dosimeter readings and factors affecting the readings are not included.
5. Failure of the quality assurance program to identify, recommend, or provide solutions for quality assurance problems and verify the implementation of such solutions, as required by 21 CFR 820.20(a)(3). This would also be a violation of the Quality System Regulation, 21 CFR 820.100 and 21 CFR 820.20(c). For example, some of the records for dosimeter readings, data sheets, and product load pattern verifications have not been properly completed for at least [REDACTED]
6. Failure of the quality assurance program to assure that all quality assurance checks are appropriate and adequate for their purpose and are performed correctly, as required by 21 CFR 820.20(a)(4). This would also be a violation of the Quality System Regulation, 21 CFR 820.20(b)(3). For example:
- a) The written procedure for reading dosimeters does not include complete instructions for quality assurance personnel, such as:
 - 1) The expected value of non-irradiated solution, maintenance of the solution, and actions to be taken if the value is out of range are not included.
 - 2) The temperature reading specification and location to be read are not included.
 - 3) Precautions to protect dosimeter readings and factors affecting the readings are not included.
 - b) Failure to always properly fill out and review irradiator cycle timer calibration records. Management signed as reviewed without comment the following:
 - 1) Not determining percent deviation [REDACTED]

- 2) Date of management review is prior to calibration check date [REDACTED]
 - 3) Standard timer calibration date is after the date the calibration check was performed, [REDACTED]
 - c) No monthly preventative maintenance, or documentation of justification, was performed on the irradiator, [REDACTED] as required by the owner's manual and written procedure.
7. Failure to adhere to a written schedule for the maintenance of equipment to assure that manufacturing specifications are met, as required by 21 CFR 820.60(a). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(g)(1). For example, no monthly preventative maintenance, or documentation of justification, was performed on the irradiator, [REDACTED] as required by the owner's manual and written procedure.
8. Failure to adequately document periodic inspections to assure adherence to applicable equipment maintenance schedules, as required by 21 CFR 820.60(b). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(g)(2). For example, no monthly preventative maintenance, or documentation of justification, was performed on the irradiator, [REDACTED] as required by the owner's manual and written procedure.
9. Failure of training programs to provide personnel with the necessary training to perform their assigned responsibilities adequately; and failure to conduct and document training programs, where training programs are necessary to assure that personnel have a thorough understanding of their jobs, as required by 21 CFR 820.25(a). This would also be a violation of the Quality System Regulation, 21 CFR 820.25(b). For example, the training program is not sufficient, in that:
- a) There is no written training program identifying areas and positions that require a thorough understanding of procedures, and verification that the personnel have received all proper training, prior to the onset of the procedures.
 - b) Master training records do not include the names of recipients of the training.
 - c) [REDACTED] has no documented training to be able to perform duties including: dosimeter readings, completing quality assurance reports and data sheets,

product load pattern verifications, coordination for dose mapping, and following dosimeter retention scales.

- d) [REDACTED] has no documentation of training received on the proper performance of preventative maintenance for the irradiator.

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 form FDA 483 issued at the close 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. If the causes are determined to be systems problems, you must promptly initiate permanent corrective 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.

During the inspection our Investigator requested that you provide a list of your consignees. You refused to provide this information. Please provide this information in your response to this Warning Letter. Failure to provide the requested information may result in regulatory action affecting all products irradiated in Malaysia for exportation to the United States including import detention.

Please notify this office, in writing, within 15 working days of receipt of this letter of the specific steps you have taken 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. Please include any and all documentation to show that adequate correction has 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.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement I, General Surgery Devices Branch, HFZ-323, 2098 Gaither Road, Rockville, MD 20850, to the attention of Mr. Joseph L. Salyer.

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In closing, given the serious nature of the violations noted above, the Food and Drug Administration is planning another inspection of Sinagama, Bangi, Kajang, Malaysia, later this year. You will be contacted by our Division of Emergency and Investigational Operations as to the scheduling of the inspection.

Sincerely yours,


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