DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service d1963b

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 1 1998

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Daniel Leiva
General Manager
DeRoyal Cientifica de Central America, S.A.
Zona Franca Metropolitana
Barreal de Heredia
COSTA RICA

Dear Mr. Leiva:

During an inspection of your firm located in Barreal de Heredia, Costa Rica, on February 9-12, 1998, our investigators determined that your firm manufactures esophageal stethoscopes with and without thermistors. These products are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices 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 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 The 1978 Good Manufacturing Practices (GMP) Regulation was superseded on June 1, 1997, by the Quality System Regulation. Since some of the records reviewed were dated prior to June 1, 1997, the deficiencies noted during the inspection are cross referenced to the 1978 GMP's.

1. 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). This would also be a violation of the GMP Regulation, 21 CFR 820.61. For example, the computerized [ ] software system used for materials and manufacturing management has not been validated.

   The March 3, 1998, response stated that DeRoyal is evaluating the [ ] software system, and all applicable modules of the [ ] software system will be validated. A specific timeframe for completion of this validation will be included in DeRoyal's report. Please provide validation documentation for this software system.

2. Failure to validate a process with a high degree of assurance according to established procedures where the process results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). This would also be a violation of the GMP Regulation, 21 CFR 820.100(a)(1). For example:

   a. The process of bonding the two components, acoustical cuff and ear piece, to the esophageal stethoscope flexible tubing has not been validated.

      The March 3, 1998, response has not addressed this issue.

   b. Both of the "Procedure for Bonding Ear Pieces to Esophageal Stethoscope Tubing" (Control #652.051.013, revision A, dated [ ]) and "Procedure for Bonding Acoustical Cuffs to Esophageal Stethoscope Tubing" (#652.051.012, rev. A, [ ]) are inadequate in that they did not specify the UV lamp intensities and conveyor belt speeds.

      The March 3, 1998, response noted that the UV lamp intensities and belt speeds shall be verified as part of the operational qualification in the full validation of the [ ] conveyor. These specifications shall be added to the appropriate bonding procedures by [ ] [ ]. Please provide these revised bonding procedures.

3. Failure to ensure that all equipment used in the manufacturing process meets specified requirements and is appropriately designed, constructed, placed, and installed to facilitate maintenance, adjustment, cleaning, and use, as required by 21 CFR 820.70(g). This would also be a violation of the GMP Regulation, 21 CFR 820.60. For example:

   a. There is no performance of installation and operation qualification studies (including protocol, data, and summary) for the [ ]ultraviolet curing conveyor system used during the bonding assembly operations.

      The March 3, 1998, response stated that a full validation of the [ ]ultraviolet curing conveyor will be performed, including an installation qualification, operational qualification, and product performance qualification. The validation shall be completed by [ ]. Please submit this validation documentation.

b. The in-house designed oven has not been qualified for the acceptable dwell time and temperature for aging the soldered wafer thermistor assemblies to relieve stresses and chemical imbalances in the thermistor parts and stabilize the thermistor contact resistance value.

The March 3, 1998, response noted that protocols shall be written for qualification of the in-house designed oven, which includes dwell time and temperature for the thermistor curing. This qualification shall be implemented by [ ]. Please provide this qualification documentation.

c. The molding machine, [ ], has not been qualified for the operation of molding connector plugs onto the esophageal stethoscopes for connection into operation room monitoring devices. In addition, the molding procedure entitled "Moldeo de Conectores por Inyeccion de Plastico" (#DCLA.MFG.008, rev. IR, [ ]) did not address the molding machine injection settings for manufacture of the connector plugs.

The March 3, 1998, response indicated that protocols shall be written for qualification of the [ ] molding machine. This qualification shall be implemented by [ ]. Please provide this qualification documentation as well as the revised molding procedure, which includes the molding machine injection settings.

4. Failure to establish and maintain adequate procedures for acceptance of incoming product, as required by 21 CFR 820.80(b). This would also be a violation of the GMP Regulation, 21 CFR 820.80(a). For example:

a. The incoming inspection and test procedures for ceramic chips do not include the specifications for resistance that the ceramic chips are tested against (less than the minimum grind-in specifications noted in the specification drawings of the [ ] thermistor and [ ] thermistor assembly), nor do they reference the "Incoming Chips Report" form being used to report chip testing results before soldering, after soldering, and after aging. In addition, the "Chip Incoming Inspection" procedure (#Q.009, rev. 2, [ ]) refers to the QC-001 "Incoming Inspection Procedure," which is no longer used.

The March 3, 1998, response noted that the "Receipt, Handling and Storage of Incoming Goods Procedure"

(#DCLA.REC.005, rev. IR, [ ]) shall be updated to include specification for resistance and reference appropriate forms. Updated procedure shall be completed no later than [ ]. Please provide this updated procedure and the updated "Chip Incoming Inspection" procedure, deleting reference of the obsolete QC-001 procedure.

b. The incoming inspection procedure for ES/EST cuffs (#DTC.REC.003, rev. A, [ ]) is not current in that referenced procedures (#DTC.REC.001 and #650.031.001) have been revised or deleted, and the report form in actual use (Form #001QC.CR) differs from the one (Inspection Report Form #652.032.001) included in the procedure.

The March 3, 1998, response noted that the #DTC.REC.003 receiving procedure shall be updated to reference correct procedure and form. Please submit the updated procedure.

c. The reports of incoming inspection and test of ES/EST cuffs only provide test results for 10 cuffs whereas 200 or more cuffs may have been sampled (e.g., Purchase Orders #670.0097 [9 FR cuff and 12 FR cuff] and #670.0095 [18 FR cuff and 12 FR cuff]).

The March 3, 1998, response noted that operators have been retrained on the quality assurance procedure entitled "Use of ANSI/ASQC Z1.4-1993" (#DCLA.QLP.004, rev. IR, [ ]), which will allow the firm to collect smaller sample sizes. A new form, more appropriate for recording results, DCLA.020, has been implemented. Please provide the new DCLA.020 form filled out and documentation of personnel training on this procedure as well.

5. Failure to establish and maintain adequate procedures to control product that does not conform to specified requirements, as required by 21 CFR 820.90(a). This would also be a violation of the GMP Regulation, 21 CFR 820.115. For example:

a. Procedures for identifying and controlling rejected in-process material (e.g., #DCLA.QLP.017, [ ]; #DCLA.QLP.020, [ ]; #DCLA.QLP.005, [ ]; #DCLA.REC.005, [ ]; #DCLA.QLP.018, [ ]; etc.) have just recently been written. However, these procedures still allow the use of older procedures (followed by and in place at the firm prior to the purchase of the firm by DeRoyal) that do not describe

the reasons for reject in a manner that would permit evaluation of the non-conformity (e.g., at soldering, distance of the chip from the wire; at grinding, shorted or open; at repair, overall length, cleanness, fitting of the cap; etc.)

The March 3, 1998, response noted that reject reasons would be redefined so as to permit evaluation of the non-conformity, and procedures would be revised as appropriate. This deficiency would be corrected by [ ]. Please submit these revised procedures.

b. Trending of nonconformities is done for scraps (not rejects). However, the scrap report, dated [ ] to [ ], is not mentioned in procedures to describe where this data is generated from, how the data is to be used, and what the acceptable scrap percentage is for each operational step.

The March 3, 1998, response noted that a procedure shall be drafted detailing how nonconformities shall be trended. This procedure shall be implemented no later than [ ], indicating where the data is obtained, how the data is used, and the acceptable percent scrap for each step. Please provide this newly established procedure.

6. Failure to address the evaluation, determination of need for an investigation, and disposition of nonconforming product as well as failure to set forth the review and disposition process in nonconforming product control procedures, as required by 21 CFR 820.90(a) and 820.90(b), respectively. This would also be a violation of the GMP Regulation, 21 CFR 820.115. For example, the procedure entitled "Control of Non-Conforming Product/Corrective and Preventive Action" (#DCLA.QLP.018, rev. IR, [ ]) does not include or reference what are the "applicable procedures" to be used to review nonconforming product for disposition. This procedure and any other related procedures do not describe how in-process or finished product (prior to packaging and labeling) nonconformities will be evaluated and investigated, nor do they describe the review and disposition process.

The March 3, 1998, response noted that the procedures shall be updated to include requirements for review of nonconforming product for disposition, and how in-process or finished product nonconformities will be reviewed, evaluated, investigated, and dispositioned. These updated procedures shall be implemented no later than [ ].

Please provide the updated procedures and documentation verifying this implementation. Also, please modify and submit the #DCLA.QLP.018 procedure to include or reference what the above-mentioned "applicable procedures" are.

7. Finished devices are released for distribution although the associated data and documentation is not reviewed; the release is not authorized by the signature of a designated individual(s); and the authorization is not dated, as required by 21 CFR 820.80(d)(2)(3)(4). This would also be a violation of the GMP Regulation, 21 CFR 820.20(a)(1). For example, acceptance records (i.e., routings documenting the assembly and testing of subassemblies and finished devices; e.g., Work Orders #[ ]) as well as rejection records (i.e., the assembler's time sheet entitled "Boleta para Control de Produccion" documenting the number of devices failing the in-process and/or finished device testing; e.g., the six assembler's time sheets recording "natural high" resistance defect, dated [ ] [ ]) are not reviewed and approved by a designated individual prior to the release of finished devices for distribution.

   The March 3, 1998, response noted that the Device History Records are now reviewed and approved by a designated individual, as detailed in the #DCLA.QLP.005 Procedure for Review of Device History Records. Please submit this modified procedure and documentation verifying this correction.

8. Failure of the device history record to include adequate acceptance records to demonstrate that the device is manufactured in accordance with the device master record, as required by 21 CFR 820.184(d). This would also be a violation of the GMP Regulation, 21 CFR 820.184. For example, the device history record for Work Order #[ ], dated [ ], does not contain any device assembly or finished device testing documentation associated with it. Also, not all device history records of Work Orders #[ ], [ ] contain the appropriate assembly and testing documentation showing that all steps were completed.

   The March 3, 1998, response has not address this issue.

9. Failure to establish and maintain an adequate procedure for defining and controlling the manner of production, as required by 21 CFR 820.70(a)(1). This would also be a violation of the GMP Regulation, 21 CFR 820.100(a)(1). For example, the procedure for grinding of the thermistors ("Esmerilado," #DCLA.MFG.007, rev. IR, [ ]), which is performed after the oven aging step, does not address or

identify the resistance specification ranges that are acceptable for the thermistor subassemblies.

The March 3, 1998, response noted that although not included in the procedures, these ohm meter allowable specifications were documented and posted at appropriate stations. The grinding procedure shall be updated to include the specifications no later than [ ]. Please provide this updated procedure.

10. Failure to establish and maintain adequate procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices meets acceptance criteria, as required by 21 CFR 820.80(d). This would also be a violation of the GMP Regulation, 21 CFR 820.160. For example, the procedure for testing of the thermistors ("Prueba de Termistores," #DCLA.MFG.013, rev. IR, [ ]), which is the final finished device testing prior to release and is conducted after the epoxying and capping stages, does not reference the resistance specification ranges that are acceptable for the thermistor subassemblies.

    The March 3, 1998, response noted that the #DCLA.MFG.013 procedure shall be updated to include reference to the ohm meter allowable specifications no later than [ ]. Please provide this updated procedure.

11. Failure to document in-process and final acceptance activities, as required by 21 CFR 820.80(e). This would also be a violation of the GMP Regulation, 21 CFR 820.20(a)(2). For example, no in-process and finished device inspection and test rejections are documented for product failures in the UV bonding area.

    The March 3, 1998, response noted that a form has been created, DCLA.011, which documents the reason for failure, are in which the failure was noted, and correction of the issue. This form will be retained with each work order as part of the Device History Record. Please submit this newly established form.

12. Failure to make available documents that are adequate and that have been established to meet the requirements of this part, as required by 21 CFR 820.40(a). This would also be a violation of the GMP Regulation, 21 CFR 820.180. For example, equipment maintenance procedures entitled "Maintenance Guide - Truematic Molding Machine" are in English, not Spanish, the native language of the person performing the maintenance. It appeared on 02/11/98, that the maintenance person did not understand the maintenance procedures.

The March 3, 1998, response noted that the appropriate maintenance procedures have been translated into Spanish. Please submit the translated procedures showing correction of this deviation.

13. Failure to maintain requirements for the personal practices where contact between such personnel and product or environment could reasonably be expected to have adverse effect on product quality, as required by 21 CFR 820.70(d). This would also be a violation of the GMP Regulation, 21 CFR 820.56(c). For example, the dress code procedure ("Politicas de Vestimenta," #DCLA.QLP.009, rev. B, [ ]) states that no chewing gum is permitted in the clean manufacturing area; however, it was observed that an employee was chewing gum in this area.

    The March 3, 1998, response noted that all employees have been retrained on the dress code procedure and educated on the importance of following the procedure. Please submit documentation of retraining employees on this procedure.

Additionally, please submit a procedure outlining a standard method for recording dates on documents maintained by the firm as promised by [ ], QA and Laboratory Group Manager, during the inspection.

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 symtomatic 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 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.

We acknowledge that DeRoyal Industries, Inc., Powell, Tennessee, has submitted to FDA a response, dated March 3, 1998, concerning our investigators' observations noted on the FDA 483 form. We have reviewed this response and have concluded that it is inadequate as described above.

Given the serious nature of these violations of the Act, the esophageal stethoscopes with and without thermistors manufactured by DeRoyal Cientifica in Barreal de Heredia, Costa Rica, may be detained upon entry into the United States without physical

examination 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.

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. Xuan T. Vo 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 Adriana Galdi

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

cc: [ ]
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