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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Food and Drug Administration
555 Winderley Pl., Ste. 200
Maitland, FL 32751

WARNING LETTER

FLA-04-32

May 11, 2004

Luis Candelario, President
Nipro Diabetes Systems, Inc.
3150 N.W. 107th Avenue
Miami, Florida 33172

Dear Mr. Candelario:

During an inspection of your establishment located at 3801 Commerce Parkway, Miramar, Florida on various dates between January 13 and February 17, 2004, FDA Investigator Dianaris Ayala determined that your firm is a specification developer of the Nipro GlucoPro Amigo™ Insulin Pump, an ambulatory pump intended for the subcutaneous infusion of insulin. This is a device as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), [21 U.S.C. 321(h)].

Our inspection revealed that these devices are adulterated within the meaning of Section 501(h) [21 U.S.C. 351(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 Quality System (QS) Regulation, Title 21, Code of Federal Regulations (CFR), part 820.

1. Your firm failed to conduct and document management reviews according to established procedures to ensure that the quality system satisfies the requirements of 21 CFR Part 820 and your firm's established quality policy and objectives, as required by 21 CFR 820.20(c). (FDA 483, Item #1).
2. Your firm failed to conduct internal audits to assure that the quality system is in compliance with established quality system requirements, as required by 21 CFR 820.22. You have not conducted internal audits according to your firm's established procedures (FDA 483, Item #1).

3. Your firm failed to conduct and document formal reviews at appropriate stages of the device's design, as required by 21 CFR 820.30(e).
 - Design reviews were not conducted at major decision points throughout the design verification/validation of the Amigo™ Insulin Pump to ensure the design meets functional, operational and other regulatory requirements. (FDA 483, Item #s 1 & 4).
 - You did not follow Procedure 02-04-S, Design Review for the Glucopro™, which requires that documented reviews of the design results be conducted at appropriate stages of the device design development. In addition, the results of the design review, including identification of the design, the date, and the individuals performing the review were not documented in the device history file (FDA 483, Item #s 4 & 5).
4. Your firm failed to establish and maintain the requirements, including quality requirements, that must be met by suppliers, contractors and consultants, as required by 21 CFR 820.50(a). Your firm failed to evaluate suppliers and contractors to ensure their adherence to the QS Regulation (FDA 483, Item #1).
5. Your firm failed to complete the design validation under defined operating conditions on initial production units to ensure that devices conform to defined user needs and intended uses, including: testing of production units under actual or simulated use conditions, software validation and risk analysis, as required by 21 CFR 820.30(g).
 - Unresolved discrepancies were reported at the completion of the design validation of the Amigo™ Insulin Pump system; for example, failures of several items of the regression test execution related to software, firmware, and pump performance and flaws in molded plastic parts and bonding of the battery cup were not addressed as part of the manufacturing and assembly issues. These issues remain open despite the fact that the design validation/verification report was approved, the process validation was initiated, and four pumps were distributed. The system and manufacturing issues include, for example:

- a) Issue #74 – Firmware did not properly detect “Position Sensor Error”.
- b) Issue #77 – Pump incorrectly saved the last 30 days worth of insulin delivery totals.
- c) Issue #78 – 10.00 U/hr Basal delivery did not meet mechanical accuracy requirements.
- d) Issue #79 – Pump s/n 00020 went into continuous reset mode when the battery was between low and dead condition. Battery voltage measures good, but cannot supply the appropriate current to run the motor.
- e) Issue #84 – System Hazard Analysis, Hardware Design Document, Software/Firmware Design System Document, Unit Test, and Integration Test documentation have not been reviewed by MTX per the System Verification/Validation Plan.
- f) Issue #94 – Allowable range for hours setting is incorrect in both 12 and 24 hour mode.
- g) Issue #5 – Battery cup to cap adhesive failure.
- h) Issue #10 – Flaws in plastics: housing, battery cap, battery endplate, IR endplate, syringe chassis, tow piece drive nut.

In addition, three units (Serial #s [REDACTED] and [REDACTED]) were returned by the contract manufacturer at your request for investigation of a nonconformance reported during assembly/testing. There is no documentation reporting that the nonconformances were investigated and closed prior to the release and distribution of the units (FDA 483, Item #2).

- At the time of the inspection, the Software Configuration Management Plan, including the Hardware Design document, the Software/Firmware Design document and the Hardware and Software Unit Integration Test document had not been completed. These records and the Risk Analysis report have not been forwarded to the contract manufacturer for their review as established in the Verification and Validation Plan (FDA 483, Item #3).

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. 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.

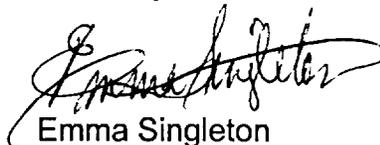
We have reviewed your response dated March 16, 2004 and acknowledge the general commitments made and the fact that some of the responses to certain FDA 483 items appear to propose adequate corrective actions. However, in general your responses appear to be specific to the cited deviations and do not take a systematic approach to comprehensively cover the corrective and the preventive actions. We also note that many of your SOPs appear to be general procedures that do not specifically address your actual products, manufacturing, quality assurance, and testing, to name a few of the systems required to assure your devices meet established quality requirements. You may find it helpful to develop SOPs that are tailored to your products. Your response to the FDA 483 has been made part of the Florida District file.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations 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 penalties. Additionally, no premarket submissions for Class III devices to which QS Regulation deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the steps you have taken to correct the noted violations, including (1) the time frames within which the corrections will be completed, (2) any documentation indicating the corrections have been achieved, and (3) 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 also advise the status of devices that have been distributed.

Your response should be sent to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, Florida 32751, (407) 475-4728.

Sincerely,

A handwritten signature in black ink, appearing to read "Emma Singleton".

Emma Singleton
Director, Florida District