



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 25 1997

WARNING LETTER
VIA FEDERAL EXPRESS

Professor Dr. Gilberto E. Bestitti
Managing Director
Disetronic Medical Systems, AG
Brunnmattstrasse 6
CH-3401 Burgdorf
Switzerland

Dear Dr. Bestitti:

The Food and Drug Administration (FDA) conducted an inspection of your firm's manufacturing facility at Burgdorf, Switzerland on November 18-21, 1996. Our investigator confirmed that you manufacture the Disetronic's H-TRON V100 infusion system, now named the H-TRONplus. This infusion system, promoted for use as an insulin delivery system for diabetes patients, is a device as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). Our records indicate that a determination of substantial equivalence (K905693) for your insulin pump called the H-TRON V100 ("H-TRON") was made in April 1993. A review of the two devices revealed that significant modifications to the H-TRON V100 pump have resulted in the new H-TRONplus device which require the submission of a 510K and a determination of substantial equivalence. Therefore, this device is misbranded within the meaning of Section 502(o) of the Act because a notice or other information respecting it was not provided as required by section 510(k) and adulterated within the meaning of Section 501(f)(1)(B) of the Act because it is a class III device under section 513(f) which is required to have in effect an approved application for premarket approval (PMA) or an approved Investigational Device Exemption (IDE) and no such PMA or IDE is in effect. In addition, the inspection revealed that your firm has Good Manufacturing Practices deficiencies regarding manufacturing, instrument calibration, and complaint handling.

510(k) submission

We reviewed your December 13, 1996, response to the November 7, 1996, and determined that your justification for not submitting a new 510(k) for changes made to the H-TRON V100 device is not adequate.

There are four categories of changes that have been made to the H-TRON V100 pump:

1. The control mechanism for the device was changed.

a) The "h" and "m" buttons were repositioned and separated by approximately [REDACTED] inch. The #1 circuit board was realigned to these new button positions.

b) The "s" button is now a [REDACTED] that utilizes [REDACTED] on the circuit board instead of a [REDACTED]. In addition, the "s" button is [REDACTED] not [REDACTED] to the device housing.

c) A new bearing is used in the motor gear box.

d) The electronic circuitry was changed by [REDACTED]

e) Error Code #11 was added.

2. The performance specifications of the device were changed.

a) Temporary increases or decreases in the basal rate are accomplished in [REDACTED] increments instead of [REDACTED] increments.

b) Basal rate increases are maintained for [REDACTED] hours, while decreases in basal rates are maintained for [REDACTED] hours. Increases and decreases are [REDACTED] hours each for the H-TRON.

c) Bolus delivery does not deactivate the temporary basal rate program.

d) Catheter fill volume is now [REDACTED] instead of [REDACTED].

e) New [REDACTED] and [REDACTED] to indicate device function and condition.

3. The software was changed, consistent with the new performance specifications.

4. The labeling was changed.

a) Pre-printed labels replace the silk-screen printing on the front of the pump and on the snap cover.

b) The Instructions for Use (User's Manual) was revised to reflect changes made to the device.

c) New brochures have been prepared.

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. In addition, your device may be detained upon entry into the United States until the premarket clearance issue is corrected.

We have reviewed your responses to the GMP observations cited on the FDA-483 given to you at the end of the inspection. A summary of that review follows:

21 CFR 820.20(a)(4)

1. 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 21CFR 820.20(a)(4). For example, the validation procedures defining the structure, documentation requirements, and the responsibilities for review and approval, have not been established for the device. This would also be a deviation of the Quality System Regulation, 21 CFR 820.20(b)(3).

21 CFR 820.61

2. Failure to validate software programs by adequate and documented testing, when computers are used as part of an automated production or quality assurance system, as required by 21 CFR 820.61. For example:

- a) The validations were not documented for the computer software used to control the in-process inspection for the motor component of the H-TRONplus;
- b) The computer software used to control the in-process testing of the LP Mainboard V 1.0 was not validated for the test performed documented.

This would also be a deviation of the Quality System Regulation, 21 CFR 820.75

21 CFR 820.100(a)(2)

3. Failure to have specification changes approved and documented by a designated individual(s) including an approval date and the date the change becomes effective, as required by 21CFR 820.100(a)(2). For example, software changes made from the H-TRON V100 to the H-TRONplus V100 have not been adequately validated in that the complete set of parameters, including all alarms, have not been tested.

This would also be a deviation of the Quality System Regulation, 21 CFR 820.30. While this is a deviation from the Quality System Regulation, at the present time, the Food and Drug Administration is giving firms until June 1, 1998 to come into compliance with this section of the Quality System Regulation.

21 CFR 820.100(b)(1)

4. Failure to have written procedures describing any processing controls necessary to assure conformance to specifications, where deviations from the device specifications could occur as a result of the manufacturing process itself, as required by 21 CFR 820.100(b)(1). For example, it was observed that when an infusion pump unit is rejected in -process, the unit is taken apart and certain components are reused/placed back into regular production. There are no written procedures for employees to follow to control whether a rejected unit met specifications.

This would also be a deviation of the Quality System Regulation, 21 CFR 820.70(a)

21 CFR 820.61

5. Failure to routinely calibrate measurement equipment, to establish adequate calibration procedures, and to maintain records of calibration, including the next calibration date, as required by 21 CFR 820.61. For example, review of the calibration and maintenance procedures and schedules revealed that the control instruments for temperature, pressure, and time have not been calibrated. Visual checks on devices alone will not ensure that equipment is operating within specifications.

This would also be a deviation of the Quality System Regulation, 21 CFR 820.70(i)

21 CFR 820.198(a)

6. Failure to review, evaluate, and maintain by a formally designated unit all records of written and oral complaints relative to the identity, quality, reliability, safety, effectiveness, or performance of a device, as required by 21 CFR 820.198(a). For example, your firm does not routinely receive complaint or MDR information unless a device is returned and requires additional technical investigation. If the product has not been received after 60days, the complaint is closed.

This would also be a deviation of the Quality System Regulation, 21 CFR 820.198(a)

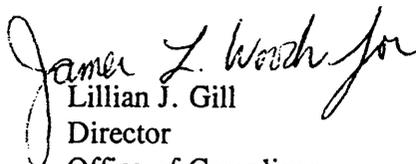
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violation noted in this letter and the deficiencies noted on the FDA-483 issued at the close-out of the inspection may be symptomatic of underlying problems in your

firm's manufacturing and quality assurance systems. We acknowledge that you have submitted responses dated December 12 and December 24, 1996, concerning our investigator's observations noted on the form FDA-483. It appears that the responses which address those observations relating to the manufacture (GMPs) of the H-Tron V100 infusion system, are adequate.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted 510 (k) violation. 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 corrections, should be included with your response to this letter. Please address your response and any questions to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement II, General Hospital Devices Branch, HFZ-333, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Ms. Carolyn Niebauer, Chief.

Should you require any assistance in understanding the contents of this letter or arranging a future inspection after corrections have been completed, do not hesitate to contact Ms. Madalyn Sheldon at the letterhead address or at (301)594-4618 ext. 121 or Fax (301) 594-4638.

Sincerely yours,


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

cc: Mr. Patrik DeHaes
President and CEO
Disetronics Medical Systems, Inc.
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