



CERTIFIED MAIL
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Food and Drug Administration
7200 Lake Ellenor Drive
Orlando, FL 32809

WARNING LETTER

FLA-98-19

January 14, 1998

Arup Sen, Chairman and CEO
Electropharmacology, Inc.
2301 N.W. 33rd Court, Suite 102
Pompano Beach, Florida 33069

Dear Dr. Sen:

We are writing to you because on September 22 through October 6, 1997 FDA Investigator Michelle S. Dunaway collected information that revealed serious regulatory problems involving the SofPulse shortwave diathermy device, which is manufactured and distributed by your firm.

Under the Federal Food, Drug, and Cosmetic Act (The Act), this product is considered to be a medical device because it is used to treat a medical condition or to affect the structure or function of the body. The law requires that manufacturers of medical devices conform with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation as specified in Title 21, Code of Federal Regulations (CFR), Part 820. The 1978 Good Manufacturing Practice (GMP) for Medical Devices regulation was superseded on June 1, 1997, by the Quality Systems regulation, which incorporates the device GMP.

The inspection revealed that the device is adulterated under 501(f)(1)(B) because the SofPulse is a Class III device under section 513(f) and does not have an approved application for premarket approval in effect pursuant to section 515(a) or an approved application for an investigational device exemption under section 520(g), and

The inspection revealed that the 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 the manufacture, processing, packing, storage or distribution are not in conformance with the Quality System Regulation. These violations include, but are not limited to the following:

- Failure to review, evaluate, and investigate any complaint involving the possible failure of a device to meet any of its specifications, e.g., of the 36 device history records reviewed based upon QC rejection during final and incoming return inspections in 1997, 17 were found to have repairs initiated as a result of a failure of the device to meet specifications. None of the 17 which did not meet specifications were processed as complaints, but rather as a standard maintenance activity.
 - a) Equipment pick-up and/or replacement form dated June 1, 1997 for a unit (s/n 1272) returned with a clock reading of 76.3 hours from "HN&R" states "Unit has no signal at all!" as the reason for returning equipment.
 - b) Device Quality Control Traveler form, dated September 12, 1997, for a unit (s/n 335) returned with a clock reading of 929.3 hours, states one of the reasons for rejection of the device during the incoming inspection as "The customer reported that sparking came out near by RF connector on the applicator."
 - c) Equipment Pick-up and/or replacement form, dated March 21, 1997 for a unit (s/n 513) returned with a clock reading of 21.6 hours from user facility "MCG" states "Applicator head makes a loud buzzing sound" as the reason for returning equipment and the MRT Device Rejection Record dated April 16, 1997 states "please see attached equipment pick-up form for a customer complaint".
- Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit to ensure that the records of investigation of any complaint include dates and results of the investigation, e.g., your complaint handling system does not include a requirement to document the dates and results of any investigation made in response to a complaint.
- Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a designated unit and to ensure that complaints are

evaluated to determine whether the complaint represents an event which must be reported to FDA under part 803 or 804, e.g., your complaint handling system does not include a method to ensure that all complaints are evaluated to determine MDR reportability.

- Failure to establish and maintain procedures that address the identification, documentation, evaluation, segregation, and disposition of nonconforming product, including a determination of the need for an investigation, for in-process, finished or returned devices. Procedures for nonconforming product only relate to the control of vendor supplied components and materials and not to in-process, finished, or returned devices.
- Failure to establish and maintain procedures for implementing corrective and preventive action which include requirements for analyzing service records to identify existing and potential causes of nonconforming product or other quality problems, to identify the actions(s) needed to correct and prevent recurrence of nonconforming product and other quality problems, to verify or validate the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, e.g., the identification and preventive actions are nonstandardized or systematic, but based on the QC Manager's experience and knowledge base. There are no written procedures related to any activity to identify correction and prevention other than vendor activities. This has resulted in not identifying or investigating the root cause for arcing in returned product s/n 315, 513, 1157, 1369, and 1414. Furthermore, you have not identified the root cause for no power output from the generator or no power complaints for s/n 1075, 1150, and 1254.
- Failure to implement and record changes in methods and procedures needed to correct and prevent identified quality problems, e.g., unit s/n 1075 was released for distribution February 27, 1996 and returned on March 29, 1996 with a clock reading of 5.3 hours because "unit not working." The repair was to replace Q202, tune applicator and calibrate the unit. The investigation revealed that the most likely cause was because the

mounting screws had not been tightened properly and caused a short. The recommended preventive action, date April 1, 1996, was to add the statement "Ensure MOSFET mounting screws are tight and not shorting to component" to the Final Amplifier Procedure. No preventive action has been completed.

- Failure to analyze service reports with appropriate statistical methodology to identify existing and potential causes of nonconforming product or other quality problems, e.g., the monthly QC inspection logs, used to identify potential causes of nonconforming product or other quality problems and to initiate corrective and preventive actions in lieu of QA review of service reports, do not always include information that lends itself to meaningful analysis. Arcing was identified on the monthly QC inspection log as a failure mode for returned product s/n 315, 513, 1157, 1369, and 1414, and "no power output from the generator" or "no power" were identified for s/n 1075, 1150, and 1254, identified with statistical data for corrective and preventive action."
- Failure to document rework and reevaluation activities in the device history record (DHR), e.g., On March 29 and 30, 1997 three different devices (s/n's 1427, 1431, and 1436) failed the final acceptance test due to arcing of the applicator meter. Consequently, these devices were reworked and retested. The initial final acceptance test and the rework activities were not documented in the appropriate DHRs, e.g., supplier PCB's and in-process subassemblies were reworked and inspected without consistent, routine documentation of the first inspection or rework activities.
- Failure to maintain a device master record (DMR) which includes device specifications, production process specifications, quality assurance procedures and specifications, labeling and packaging specifications, and to ensure that each DMR is prepared and approved in accordance with section 820.40. The following changes to the DMR were not documented or formally approved prior to implementation:

- a) the Faraday shield upgrade referenced in QC inspection reports dated October 22, 1996 did not receive final documentation and approval until January 15, 1997;
 - b) the modification of the end of the RF copper coil from a sharp edge to a rounded edge occurred March 1997, however, this change has never been formally documented or approved;
 - c) the modification to the amount and placement of glue used to affix the applicator cover to the applicator housing occurred in November or December 1996, however, this change was never formally documented or approved;
 - d) the modification of adding acrylic insulation inside the applicator occurred in 1994, but this change was never formally documented or approved; and
 - e) all labeling is not included as part of the DMR and all changes are not formally documented or approved.
- Failure to include, or refer to the location of all current device specifications, production process specifications, quality assurance procedures and specifications, and packaging and labeling specifications in the Device Master Record (DMR), e.g., current information relating to the applicator RF coil, applicator housing glue and applicator acrylic insulation has not been included in the SofPulse DMR.
 - Failure to establish procedures for quality audits and conduct such audits to assure that the quality system is in compliance with the established quality system requirements, e.g., there has not been an internal audit of the complaint handling and MDR systems conducted since March 20, 1996. The procedure states that the audit checklist should be used to perform audits semi-annually, however, there was no checklist. The last quality audit was an ISO audit that was conducted in March 1997, however, it did not include an audit of the complaint handling and MDR systems.

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The SofPulse is misbranded within the meaning of section 502(o) of the Act in that a notice or other information respecting the SofPulse device was not provided to the FDA as required by section 510(k) of the Act, and 21 CFR 807.81(a)(3)(ii) for major changes or modifications in the intended use of the device, including but not limited to: Carpal Tunnel Syndrome; edema following CVA; cellulitis; pain management; rehabilitation from stroke or surgery; wound management; pressure or decubitus ulcers; sprains and fractures; post-operative pain after ankle arthrodesis; post-operative pain after soft tissue reconstruction or nerve grafting; tissue repair by affecting cell to cell communication, cell locomotion, extracellular matrix synthesis, vascularization or stimulation; and modulating biological processes associated with injured or inflamed tissue.

The SofPulse is also misbranded within the meaning of section 502(t)(2) in that your firm failed to furnish material or information required by or under section 519 and the Medical Device Reporting Regulation, 21 CFR Part 803, as follows:

- Failure to have written MDR procedures that reflect current Medical Device Reporting requirements, e.g., document RA00-004, dated April 30, 1996, does not reflect current MDR requirements, and includes a form other than MedWatch Form 3500A (which includes all of the data elements required by 21 CFR Part 803.52.).

Our review of promotional literature used by your firm to promote the SofPulse device found the following:

The case study entitled Treating Pain Associated with Carpal Tunnel Syndrome with the SofPulse, promotes your device for the new indications of "Carpal Tunnel Syndrome", "wounds", "cellulitis", "stroke" and "pressure ulcers".

The case study entitled Ankle Reconstruction After Gun Shot Wound promotes your device for the new indications of "nerve regeneration", "wounds", "cellulitis", "stroke" and "pressure ulcers".

The brochure entitled Adjunctive Therapies promotes your device for the new indication of "pressure ulcer healing".

The brochure entitled SofPulse promotes your device for the new indications of "wounds, burns, sports injuries and fractures, cellulitis, stroke and pressure ulcers."

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Three other case studies promote your device for the new indications of the treatment of pain and edema resulting from injury, acceleration of a patient's return to function and acceleration of tissue recovery from operative trauma.

The brochure entitled DIRECTIONS FOR USE claims "Edema or pain resulting from trauma is best managed by the SofPulse when the therapy is employed as soon as possible following injury."

The videotape entitled Epi-SofPulse promotes your device for the new indications of pressure, venous insufficiency and diabetic ulcers; carpal tunnel syndrome; full and partial thickness grafts; mastectomies; neuromas; burns; lower back pain; sciatic nerve inflammation; contusions; scleritis; cellulitis; lymphedema and left hip fractures.

At the close-out of the inspection, Dr. Sen stated that EPI would no longer distribute any promotional materials that made reference to intended uses other than for the adjunctive use in the palliative treatment of post-operative pain and edema in superficial tissue. He also added that EPI had removed the promotional materials that described case studies which implied the device was safe and effective for treatment of wound and Carpal Tunnel Syndrome from their web site. A December 15, 1997, review of EPI's promotional materials by the Center for Devices and Radiological Health at www.ephi.com/science.html revealed that the same materials are still available.

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 in the FDA 483 issued to you 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 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. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

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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.

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. 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.

Responses received from you, dated October 18 and November 3, 1997 are inadequate to address the concerns from the September 22 through October 6, 1997 inspection. You must provide written documentation of policies and procedures to substantiate that corrective action has been implemented.

The checklist that you provided in your November 3, 1997 response to address the internal audit procedure does not assure that the quality system is in compliance with the established quality system requirements, nor does it determine the effectiveness of the quality system. The checklist repeats the requirements, but does not show how the specifications for the different processes (#7) are being met. This response is inadequate.

Your revised Promotional Labels and Labeling Control Procedure included in your November 3, 1997 response to address the omission of the labeling specifications in the DMR (#6B) requires explanation, e.g., more explanation is needed for how the labels will be stored (5.) and how the Sales and Marketing Department and all operating departments involved are expected to proceed with the removal of obsolete or misleading materials (5.11) which are already distributed. In addition, the document "Pulsed Electromagnetic Signals" submitted in your November 3 response suggested or made reference to numerous uses other than "adjunctive use in the palliative treatment of post-operative pain and edema in superficial tissue." This response is inadequate.

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Your response should be directed to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 7200 Lake Ellenor Drive, #120. Orlando, Florida 32809, or call (407) 648-6823, ext. #264.

Sincerely,

A handwritten signature in black ink, appearing to read "Edward R. Atkins". The signature is written in a cursive style with a prominent initial "E".

Edward R. Atkins
Acting Director
Florida District