



Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Patrick L. Johnson
Principal Product Regulation Manager
Drug Delivery Business
Medtronic, Incorporated
Neurological Division
800 53rd Avenue Northeast
Minneapolis, Minnesota 55421

JUL 21 2000

Re: P990034

Medtronic® IsoMed® Constant Flow Infusion System:
Model 8472 IsoMed® Implantable Constant Flow-Infusion Pump
Model 8543 IsoMed® Side Catheter Access Port Kit
Model 8545 IsoMed® Side Catheter Access Port Kit
Model 8553 IsoMed® Refill Kit
Model 8555 IsoMed® Refill Kit
Filed: June 28, 1999
Amended: August 20, November 5 and 22, and December 9, 1999, January 10 and 24, February 1 and 11, April 14, June 8, 12, 19, and 29, and July 13, 2000

Dear Mr. Johnson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Medtronic® IsoMed® Constant Flow Infusion System (system). This device is indicated for use when patient therapy requires the chronic infusion of approved drugs or fluids. The drugs or fluids approved for use with the system include:

1. The chronic, intrathecal infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain. A 0.9% solution of preservative-free Sodium Chloride Injection, USP, can be used to achieve the physician-prescribed concentration of preservative-free morphine sulfate sterile solution.
2. The chronic, intravascular infusion of floxuridine (FUDR) for the treatment of primary or metastatic cancer. Bacteriostatic water or physiological saline can be used to achieve the physician-prescribed concentration of chemotherapy drugs or to flush the pump reservoir.

Saline or heparinized physiological saline, unless contraindicated, may be used during an interruption in chemotherapy to maintain catheter patency.

Refer to the appropriate drug labeling for a complete list of indications, contraindications, warnings, precautions, dosage and administration information, and screening procedures.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, a postapproval report must be issued no later than six months following approval of this PMA, which contains results from two additional test cycles of your recently revised steam sterilization process. The protocol for this revised process is defined in your Medtronic Process Validation Plan QAD00-0492 (Rev B), which was previously supplied in Amendment A010 (received on June 8, 2000).

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Page 3 - Mr. Johnson

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

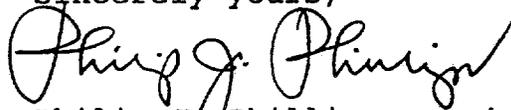
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. As part of our reengineering effort, the Office of Device Evaluation is piloting a new process for review of final printed labeling. The labeling will not routinely be reviewed by FDA staff when PMA applicants include with their submission of the final printed labeling a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment. Please see the CDRH Pilot for Review of Final Printed Labeling document at <http://www.fda.gov/cdrh/pmat/pilotpmat.html> for further details.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Mr. William M. Burdick at (301) 594-1287.

Sincerely yours,



Philip J. Phillips
Deputy Director for Science
and Regulatory Policy
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Issued 3-4-98

CONDITIONS OF APPROVAL
FOR CARDIAC PACEMAKERS AND PROGRAMMERS

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Boulevard, Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Boulevard, Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

In addition to the above and in order to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use, the annual postapproval reports shall include, separately for each model number (if applicable), the following information known by or reported to the applicant:

(1) The number of pacemakers domestically implanted and the number of reported explants and deaths.

(2) A breakdown of the reported deaths into pacemaker related and non-pacemaker related.

(3) A breakdown of the reported explants into the numbers reported at end of battery life, having complications unresolvable by programming and for other reasons with safety and effectiveness issues which can be derived from the reports stated.

(4) The number of pacemakers returned to the applicant for cause from domestic sources with a breakdown into the numbers currently in analysis, operating properly, at normal battery depletion and failed, with the failure mechanisms described.

(5) A cumulative survival table for the pacemakers.

(6) The number of programmers and modules shipped and the number of returns with a breakdown into the numbers currently in analysis, operating properly and failed, with the failure mechanisms described.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center

(HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Boulevard, Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mix-up of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of

information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc. Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

JUL 21 2000

Medical Device Tracking Order

Patrick L. Johnson
Principal Product Regulation Manager
Drug Delivery Business
Medtronic, Incorporated
Neurological Division
800 53rd Avenue Northeast
Minneapolis, Minnesota 55421

RE: Infusion Pump (P990034)

Dear Mr. Johnson:

You are notified by this letter of your obligation to adopt a method of tracking for the devices referenced above, as authorized by section 519(e) of the Federal Food, Drug, and Cosmetic Act, (the Act) as amended by section 211 of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The implementation of section 519(e) of the Act, as amended, requires the Food and Drug Administration (FDA) to issue an order to manufacturers when FDA determines that a person who manufactures and distributes a device meets the relevant statutory requirements and tracking is required to protect the public health. This order is effective immediately.

Section 519(e) of the Act, as amended, states that FDA, "...may by order require a manufacturer to adopt a method of tracking a class II or class III device—

- (A) the failure of which would be reasonably likely to have serious adverse health consequences; or
- (B) which is—
 - (i) intended to be implanted in the human body for more than one year, or
 - (ii) a life sustaining or life supporting device used outside a device user facility."

As you know, the corresponding medical device tracking regulations, found in Title 21 Code of Federal Regulations (CFR) Part 821, are intended to ensure that tracked devices can be traced from the device manufacturing facility to the person by whom the device is

intended to be used when patient notification (under section 518(a) of the act) or device recall (under section 518(e) of the act) actions are ordered by the agency. The device tracking requirements for exemptions and variances, system and content requirements of tracking, the obligations of persons other than device manufacturers, such as distributors, records and inspection requirements, confidentiality, and record retention requirements, which were published in the **Federal Register** on August 16, 1993, remain in effect. (21 CFR sections 821.2, 821.25, 821.30, 821.50, 821.55 and 821.60, copy enclosed.)

This order to adopt a tracking method does not change your obligations concerning other existing FDA regulations affecting your device. FDA may publish in the **Federal Register** further announcements concerning your device or the medical device tracking requirements under 21 CFR Part 821. Please contact Chet Reynolds in the Office of Compliance at (301) 594-4618 if you need specific guidance. Other general information on your responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking, may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at the internet address www.fda.gov/cdrh.

Sincerely yours,

Steven M. Niedelman
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosure

R/T-/F/T: C Uldriks 7/22/00

Cc: HFA-224
HFZ-404
HFZ-300
HFR-MW-300