DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Room –WO66-G609
Silver Spring, MD 20993-0002

FEB - 7 2012

Ms. Jill Schweiger
Vice President, Clinical Studies and Regulatory Affairs
Medasys, Incorporated
500 International Drive
Suite 200
Mount Olive, New Jersey 07828

Re: P080012
Prometra Programmable Infusion Pump System
Filed: April 11, 2008
Amended: June 9, 2008; June 18, 2008; June 30, 2008; September 5, 2008; September 8, 2008; November 26, 2008; January 15, 2009; March 16, 2009; April 10, 2009; June 16, 2009; November 2, 2009; November 23, 2009; March 11, 2010; December 8, 2010; January 31, 2011; July 25, 2011; and November 30, 2011
Procode: LKK

Dear Ms. Schweiger:

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 Prometra Programmable Infusion Pump System.

The Prometra Programmable Infusion Pump System is indicated for intrathecal infusion of Infumorph (preservative-free morphine sulfate sterile solution) or preservative-free sterile 0.9% saline solution (Sodium Chloride Injection, USP).

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). FDA has determined that this restriction on sale and distribution is necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for the Prometra Programmable Infusion System has been established and approved for each separately packaged component as follows:

- Prometra Pump: 2 years
- Intrathecal Catheter Kit: 2.75 years
- Catheter Access Port Kit: 4.91 years
- Pump Refill Kit: 4.91 years
- Tunneler Kit: 4.91 years

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below.

1. As a condition of approval, you have agreed to conduct the post-approval studies (A prospective, non-randomized, open-label, multicenter study to evaluate the long-term safety of the Prometra Programmable Pump System). The PAS protocol includes, but is not limited to the following items:

   a. It will be performed at up to 30 centers in the US.

   b. A total of 400 subjects will be enrolled to ensure at least 300 will be followed for five years.

   c. The primary endpoint is to assess the 5-year rate of granuloma formation. The primary hypothesis is that the 5-year granuloma rate is less than 3% (with a 3% margin). Secondary endpoints are to assess the long-term device performance including: (1) Pump failure (time to occurrence, type, and number of occurrences), (2) pump battery life, (3) device-related-adverse events, and (4) device-related serious adverse events. The study will also include a descriptive evaluation of the effect of race and ethnicity on granuloma formation, and the effect of alternative

drugs on granuloma formation.

d. The study participants will consist of two groups: (1) Group A: newly enrolled study subjects, and (2) Group B: subjects previously enrolled in the PUMP I or PUMP II study. Approximately 25% patients enrolled in PUMP I and PUMP II studies will be enrolled into Group B. Subjects shall be seen at least once every 90 days (± 30 days) from the date of implantation (Group A) or PAS enrollment (Group B) throughout the study.

2. As a condition of approval, you have agreed to conduct the following non-clinical post-approval studies: Post-Approval Extended Use Stability (Rev C) and Post-Approval Leachables (Rev C). This PAS is a non-clinical study to evaluate the long-term interactions between your device system and the indicated drug product. The protocols include, but are not limited to, the following items:

   a. The primary objectives of the studies are to demonstrate:

      Extended Use Stability Study

      i. Stability of Infumorph in Prometra infusion pumps for a period of 90 days;

      ii. Stability of Infumorph after multiple refills over the lifetime of the pump (10 years) in the pump reservoir; and

      iii. Pump function by assessing pump flow rate throughout study duration.

      Leachables Study

      iv. To perform controlled extraction studies to assess acceptable limits of any identified leachable materials (in consideration of the ICH Q3B and PQRI publication "Safety Thresholds and Best Practices for Extractables and Leachables in Orally Inhaled and Nasal Drug Products.")

      v. In parallel with the activities performed in accordance with the controlled extraction study, samples will be placed within the appropriate chambers and pulled at the appropriate time points. Samples at each pull point will be stored and placed for routine testing once the methods are established from the controlled extractable study.

   b. Study Samples: Sixteen (16) Prometra pumps will be included in the Extended Use Stability study. Eight (8) Prometra pumps will be included in the Leachables study.

c. Endpoints:

Extended Use Stability Study

i. Assay will be compared to a control solution at each time point.

ii. Related substances, unknown impurities, appearance and pH will be reported. Related substances and unknown impurities will be assessed for safety impact at each time point.

iii. As the study progresses, appropriate criteria for identified degradation products will be established in accordance with ICH Q3B and PQRI recommendations and will be supported with appropriate safety justifications. The established specifications will be submitted to FDA for evaluation.

iv. Flow rate accuracy shall be within ±15% of the set point at each timepoint.

Leachables Study

v. Results from leachable analysis over the sample periods will be assessed for safety impact at each time point.

vi. As the study progresses, appropriate criteria for the identified leachables will be established in accordance with ICH Q3B and PQRI recommendations and supported with appropriate safety justifications. The established specifications will be submitted to FDA for evaluation.

d. The overall study duration will be 126 months after FDA's PMA Approval, which includes the analysis and submission of the Final Study Report.

Please be advised that the results from this study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

FDA would like to remind you that you are required to submit PAS Progress Reports every six months during the first two years and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. The progress reports will include results and analysis of testing conducted on samples at time points preceding the progress report. Deviations should also be identified in the progress reports. Two copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies. Your PMA supplement should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" at the web site stated above.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (www.fda.gov/MedicalDevices /DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

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 would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR

806.10(a)(2). Additional information on recalls is available at www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, 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 www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 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 submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

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. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by 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.

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. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm; clinical and statistical data: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm)

U.S. Food and Drug Administration
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If you have any questions concerning this approval order, please contact LCDR Alan M. Stevens at 301-796-6294.

Sincerely yours,

Anthony D. Watson

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Director
Division of Anesthesiology, General Hospital,
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