July 30, 2025

Alexis Dineen
Vice President, Regulatory Affairs
25101 Rye Canyon Loop
Valencia, California 91355

Re: P240039
Trade/Device Name: SetPoint System
Product Code: SFJ
Filed: November 4, 2024
Amended: February 28, 2025, April 29, 2025

Dear Alexis Dineen:

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 SetPoint System. This device is indicated for use in the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response, loss of response, or intolerance to one or more biological or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs). Based upon the information submitted, the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

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). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device and insofar as the sale and distribution of the device are restricted to practitioners trained by SetPoint Medical training representatives. FDA has determined that these restrictions on sale and distribution are 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 all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 12 months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the 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. This report, identified as "Annual Report" 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 must 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 PMA device, under 21 CFR 814.82(a)(9), 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.

You have agreed to provide the following non-clinical information in a report, which may be followed by a PMA supplement where applicable.

1. SetPoint Medical (SPM) will provide information to FDA regarding the training and training materials for the SetPoint System as follows:
    a. The training and training material provided to:
        i. The on-site SetPoint Medical representatives that will be present for each surgeon's first five (5) implantation procedures;
        ii. Surgeons and supporting surgical/operative staff; and
        iii. Patients and prescribers regarding charging procedures and identifying when the device is functioning properly.
    b. If any involved person is trained without any written materials, a description of the manner in which this training will occur in a real-world context.
    c. Documentation of training that includes the date, purpose, method(s), and the name, professional experience and qualifications of SPM representatives and surgical attendees, and performance (e.g., Pass/Fail, Complete/Incomplete) of surgical attendees.

Be advised that failure to comply with any post-approval requirement, including providing the training and training materials, descriptions of training conducted without written training materials, and performance documentation for surgical attendees constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 21 CFR 814.46(a)(2).

You must obtain approval of your post-approval study (PAS) protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study described below. Your PMA supplement should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below and submitted 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.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

2. SetPoint Medical will conduct a SetPoint System Safety and Performance Post-Approval Study to monitor safety and technological performance to further support the safety and effectiveness of device

design changes made after completion of the pivotal study and to validate adequate real-world use of the final, finished device outside of the controlled environment of a clinical study. Specifically, this study will involve the following:

a. Creation of a registry of patients implanted with the SetPoint System, the prescribing physician and the implant/explant surgeon to enable systemic tracking and analysis of this real-world data (RWD);

b. The registry should be set up to collect the following patient, physician, surgeon, and device information and data:
    i. Patient age and sex
    ii. Other appropriate demographic information such as duration of patient's rheumatoid arthritis (RA) diagnosis and history of patient's past RA treatment
    iii. Rheumatologist identifier and experience
    iv. Surgeon identifier and general vagus nerve surgery experience level
    v. Identification of SetPoint implant procedure training and number of prior SetPoint implant procedures completed
    vi. Implantation site and date
    vii. SetPoint representative assigned to procedure (if applicable)
    viii. Device serial number and lot number
    ix. Whether cauterization needed to be used, or other intraoperative complications/deviations from standard procedure
    x. Whether the device required replacement and the reason (e.g., cauterization needed to be used)
    xi. Device performance monitoring
        1. Battery status and chargeability at time of implant activation and onwards
        2. Connectivity problems
        3. Programming difficulties
        4. Periods of non-functionality or unplanned treatment interruption
        5. Patient-reported complaints regarding charging or device function
    xii. Patient clinical outcomes relative to device performance monitoring collected every 6 months for a 3-year reporting period;

c. Enrolling an adequate number of patients to: 1) track adverse events (AEs) and device deficiencies associated with procedure deviations, 2) provide an adequate sample size to demonstrate mitigation of device failures, and 3) track adverse events associated with device failures. The registry should include an adequate number of experienced surgeons who have completed at least 5 unsupervised SetPoint System implantation procedures;

d. Monitoring deviations in clinical procedures and device use, including but not limited to, procedural mistakes, patient misunderstanding, and unplanned extended periods without treatment delivery;

e. Tracking instances where cauterization within 2 cm of the implant is required and implementation of proactive implant replacement protocols;

f. Submitting reports within 10 working days of SetPoint becoming aware of instances requiring device replacement due to cauterization within 2 cm of the device, or a device deficiency requiring intraoperative replacement or post-operative explantation; and

g. Collecting data continuously from all ongoing SetPoint System implantation procedures in the registry and submitting reports every six months during and after enrollment, for up to 3 years.

From the date of study protocol approval, you must meet the following timelines for the SetPoint System Safety and Performance PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of the SetPoint System Safety and Performance PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report within three (3) months of study completion (i.e., last subject's last follow-up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including initiation and completion of the SetPoint System Safety and Performance PAS as outlined above, timely submission of the study protocol within 60 days, submission of immediate reports for device replacements due to cauterization or malfunction, and submission of periodic PAS Progress Reports, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

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 in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post-Approval Studies Program Database Webpage, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Under 21 CFR 814.39, any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by Premarket Approval Application Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA 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. Additional information about changes that may require a PMA supplement are provided in the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 for devices or post-marketing safety reporting (21 CFR Part 4, Subpart B) for combination products, 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

https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR Part 4, Subpart B) for combination products, 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 https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

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 at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. 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 a copy of all final labeling. Final 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 labeling is identical to the labeling approved in draft form. If the final 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, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Lance Harmer at Lance.Harmer@fda.hhs.gov.

Sincerely,

David P. Mc Mullen -S

Digitally signed by David P. Mc Mullen -S
Date: 2025.07.30 20:47:15 -04'00'

David McMullen, MD
Director
OHT5: Office of Neurological and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health