DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

April 30, 2014

Mr. Joel Aaberg
Director of Regulatory Affairs
Inspire Medical Systems, Inc.
9700 63rd Avenue North, Suite 200
Maple Grove, MN 55369

Re: P130008
Inspire Upper Airway Stimulation (UAS)
Filed: May 17, 2013
Amended: September 5, 2013, October 3, 2013, October 29, 2013
Procode: MNQ

Dear Mr. Aaberg:

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 Inspire Upper Airway Stimulation (UAS) system, which includes the Model 3024 Implantable Pulse Generator, the Model 4063 Stimulation Lead, the Model 4323 Sensing Lead, the Model 2740 Physician Programmer, and the Model 3032 Patient Programmer. The device is used to treat a subset of patients with moderate to severe Obstructive Sleep Apnea (OSA) (Apnea-hypopnea Index [AHI] of greater or equal to 20 and less than or equal to 65). Inspire UAS is used in adult patients 22 years of age and older who have been confirmed to fail or cannot tolerate Positive Airway Pressure (PAP) treatments (such as continuous positive airway pressure [CPAP] or bi-level positive airway pressure [BPAP] machines) and who do not have a complete concentric collapse at the soft palate level.

PAP failure is defined as an inability to eliminate OSA (AHI of greater than 20 despite PAP usage) and PAP intolerance is defined as:

(1) Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night), or

(2) Unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it).

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). 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. 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 the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device (implantable pulse generator and leads) has been established and approved at 2 years. 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 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" 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). In addition to the conditions outlined above, you must conduct two post-approval studies as described below:

1. *Extended Follow-up of the Premarket Cohort (Inspire 4 STAR Trial):* This study will be conducted as per protocol dated December 28, 2011, Version 9.1. This is a prospective, single arm cohort study to evaluate the long-term safety of the device in 124 subjects implanted with the Inspire UAS system under the premarket study. The subjects will be followed 5-years post procedure. Any adverse events will be summarized by seriousness, severity, relatedness to the device and temporal relationship to the procedure. Data will be analyzed in a descriptive fashion using 95% confidence limits for the estimates.

2. *New Enrollment Study:* This study will be conducted as per protocol dated March 19, 2014, Version 1.5. This is a multi-center, prospective, single arm cohort study to evaluate long-term device safety and effectiveness. Accounting for a 10% attrition rate, a total of 127 subjects will be implanted with the Inspire UAS system and enrolled in the study. The study will also evaluate effectiveness of physicians' training program in a postmarket setting. The subjects will be followed 5-years post-procedure. Safety

endpoints will be collected to evaluate: long-term device-related serious adverse events, therapy-specific adverse events (i.e., stimulation discomfort, tongue abrasions weakness and deviation) at 12 months, and long-term therapy-related adverse events.

Physician training measures of post-operative safety outcomes must include surgical times, post-operative pain recovery, procedure related adverse events, and post-operative comments. Effectiveness endpoints to evaluate quality of life measures using Epworth Sleepiness Scale (ESS) and Functional Outcomes of Sleep Questionnaires (FOSQ) will be collected annually. The study must be powered to assess if the mean score at 12 months post-implant is less than 10 for ESS and more than 2 for FOSQ. Therapy efficacy measured by Apnea Hypopnea Index (AHI), Oxygen Desaturation Index (ODI) should be evaluated by using mean differences compared to baseline using single night in-lab Polysomnography (PSG) at 3 years, while two-night home sleep testing (HST) would be conducted for descriptive purposes at 2, 4, and 5-year follow-up visits. Subjects must be evaluated at baseline, during implant, at 1-, 2-, 6- and 12-months post-implant, and every six months thereafter through 5 years of post-implant follow-up.

A one-sided binomial exact test will be used to test if long term device related serious adverse events is less than a performance goal of 24% at 5 years. For therapy-specific adverse events non-inferiority test with a margin of 5% using the Bayes Factor at 12 months post implant will be used. All therapy- and procedure-related adverse events will be described and summarized by seriousness, severity, relatedness, and temporal relationship to the device and/or procedure.

Please be advised that the results from these studies 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 asked to submit separate PAS Progress Reports. For condition of approval no.1 (Extended follow-up of the premarket cohort) you will submit annual PAS reports through study completion. For condition of approval no.2 (New Enrollment) you will submit reports every six months during the first two years of the study and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, 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" (www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#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.

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 6 copies, 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
PMA Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Amy LeVelle at 301-796-6963.

Sincerely yours,

Markham C. Luke -S

For Christy Foreman
Director
Office of Device Evaluation
Center for Devices and Radiological Health