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

May 3, 2013

Ms. Neelu Medhekar
Director, Regulatory Affairs
Ethicon Endo-Surgery, Incorporated
4545 Creek Road, ML #110
Cincinnati, Ohio 45242

Re: P080009
SEDASYS® Computer-Assisted Personalized Sedation System
Filed: March 25, 2008
Amended: May 5, 16, 20 and 27, August 4 and 25, and September 5, 2008; January 21, February 25, March 16 and 30, June 25, and December 22, 2009; January 15 and 26, and September 16 and 17, 2010; November 28, and December 5, 2011; February 23 and 28, March 28, July 2, 19, 24, and 26, August 15, September 4, October 1 and 3, November 8, 2012; February 11 and 21, 2013
Procode: PDR

Dear Ms. Medhekar:

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 SEDASYS® Computer-Assisted Personalized Sedation System. This device is indicated for the intravenous administration of 1% (10 mg/mL) propofol injectable emulsion for the initiation and maintenance of minimal to moderate sedation, as defined by the American Society of Anesthesiologists (ASA) Continuum of Depth of Sedation, in ASA physical status I and II patients ≥ 18 years old undergoing colonoscopy and esophagogastroduodenoscopy (EGD) procedures.

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. Specifically, the device labeling must include the requirement that the member of the physician-led team who is administering sedation must have training in the management of the cardiorespiratory effects of propofol when administered using computer-assisted personalized sedation systems. The device labeling must also state that the training must include: (1) pharmacology of propofol, (2) identification of high risk patients, (3) recognition of progression of levels of sedation, and actions necessary to return a patient to intended levels of sedation, (4) use of capnometry and the determination of adequate ventilation and (5) management of airway obstruction and hypoventilation. In addition, the use of the device is restricted to settings where a practitioner

trained in the administration of general anesthesia is immediately available to the user for assistance or consultation as needed. Immediate availability in this context means that an anesthesia professional will be available on site to respond to an emergency situation. In order to ensure that the use of the SEDASYS System is restricted to the practitioners and settings defined above, FDA expects that Ethicon Endo-Surgery, Inc. (EES) will include the requirement to have an anesthesia provider's immediate availability be stated within the contract with each of the accredited facilities carrying the device. In addition, the device labeling will specifically state that the SEDASYS System must only be used in hospitals and/or healthcare facilities where an anesthesia professional is immediately available for assistance or consultation as needed.

Expiration dating for the SEDASYS Drug Delivery Cassette and Oral/Nasal Cannula 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 Annual Report requirements, you must provide the following data in post-approval study reports (PAS). Two (2) copies, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. You have agreed to conduct and provide the results of two (2) post-approval studies intended to demonstrate that the SEDASYS System is safe for use in clinical practice without the need for immediate availability of a trained anesthesia professional. The data from these studies will be used to consider removal of the restriction for use concerning immediate availability of an anesthesia professional. The two (2) agreed-upon post approval studies are as follows:

1. Post-Approval Study of the SEDASYS System User Response to System Alarms: This study will be conducted as per study protocol version CI-13-000X, dated March 29, 2013 (e-mailed). The study will evaluate if the SEDASYS System can be used safely in routine clinical practice, by measuring the trained users' responses to System alarms. In addition, data from this study will be used to determine if the Restriction of Use that limits use of the SEDASYS System to settings where an anesthesia professional is immediately available can be removed. This is a single arm, non-randomized, non-blinded, multi-center,

prospective, study of sedation during colonoscopy and EGD, performed in routine clinical practice.

Accounting for a 3% patient dropout a total of 866 subjects will be enrolled. The primary endpoint will be the percentage of documented responses to alarms. The secondary endpoint will be sufficiency of response and all hands-on airway rescue interventions by anesthesia professionals. Subject data will be collected prior to and during use of SEDASYS System through discharge. Subjects will be followed for one day after the procedure. Severe Adverse Events will be followed to resolution. Data collection will include complete real-time documentation of all episodes in the entire enrolled population where $SpO_2 \leq 92\%$ (yellow alarm) and/or $SpO_2 \leq 85\%$ (red alarm) occurs and clinical responses to these events. An acceptable clinical response will be considered to be both an emergent patient assessment for a yellow alarm and a therapeutically appropriate intervention for a red alarm. A Data Safety Monitoring Board (DSMB) is required in order to capture and assess any adverse events in a timely fashion. The DSMB should be comprised of independent physicians; and regular meetings should be scheduled to monitor early events. The response rate to alarms is expected to be 100%. Confirmation of a non-response will be determined by the Endpoint Adjudication Committee (EAC). If there is a single confirmed failure to respond to an alarm, the aforementioned Restriction of Use may not be removed. Confirmed non-responses will be sent to the Agency within 15 days of the EAC notifying the sponsor.

Data collection will include complete real-time documentation of all interventions needed to assist or maintain spontaneous ventilation, including routine maneuvers (e.g., chin lift, repositioning of the head). All interventions where an anesthesia professional had to perform a hands-on airway rescue intervention due to over-sedation, following inability of the gastroenterologist-led team to successfully manage the patient's airway/respiration, will be captured and details of these cases will be collected.

Documentation of response will be summarized with counts and percentages. Descriptive statistics will be provided for all failures leading to injury, adverse events and severe adverse events. The true proportion of sufficiency of response will be estimated with 95% confidence intervals using exact binomial methods. Additional endpoints will be summarized with descriptive statistics as appropriate for continuous or categorical measures.

2. Post-Approval Study of the SEDASYS System in Routine Clinical Practice: This study will be conducted per protocol version CI-13-000Y, dated March 29, 2013 (e-mail). The study will provide additional assurance that the SEDASYS System can be used safely in routine clinical practice. The primary endpoint assesses the total number of anesthesia professional rescue interventions. The secondary endpoint assesses the total number of patients sedated with the SEDASYS System requiring bag-mask ventilations (BMV) and/or artificial airway interventions (AAI). All adverse events (AEs) and serious adverse events (SAEs) will be reported and classified as unrelated or related to SEDASYS System sedation. Data from this study will be used to determine if the Restriction of Use, which

limits initial use of the SEDASYS System to settings where an anesthesia provider is immediately available, can be removed.

A total of 7,430 subjects will be initially enrolled and will provide 99% confidence that the actual proportion of anesthesia professional rescue interventions does not exceed 1/1,000. The secondary endpoint will be assessed using a one-sided exact binomial test for a proportion and a 0.025 level of significance will be used. In the event a case involves an anesthesia professional rescue intervention, a root cause analysis will be conducted by the sponsor and reviewed by FDA. If the first intervention was determined to be a result of a deficiency related to the training program, the aforementioned Restriction of Use may not be removed. If the first anesthesia professional rescue intervention was determined to be required irrespective of the training program, the study can continue. However, if two or more interventions by an anesthesia professional occur, the primary endpoint has failed and the Restriction of Use may not be removed. The sale of the SEDASYS System will be limited to facilities that have an anesthesia professional immediately available.

All interventions where an anesthesia professional had to perform a hands-on airway rescue intervention due to over-sedation, following inability of the gastroenterologist-led team to successfully manage the patient's airway/respiration, will be captured and details of these cases will be collected.

The proportion of subjects sedated with the SEDASYS System requiring BMV and/or AAI will be estimated with 95% confidence interval. The hypothesis will be tested using a one-sided exact binomial test for a proportion and a 0.025 level of significance. Descriptive statistics will be provided for adverse events, and narratives will be provided for the events.

The root cause analysis will be performed for all anesthesia professional rescue interventions and serious adverse events. The outcome of this analysis will be shared with the Agency within 15 days of the event. All adverse event case report forms will be consolidated into listings and/or tables for submission to the FDA by EES in a status report every six months from the first subject enrolled until the last subject completed.

FDA would like to remind you that you are asked to submit separate PAS Progress Reports every six months during the first two years for the first study and annually thereafter until completion of both studies. 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/DeviceApprovalsandClearnaces/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 Mr. Sugato De, M.S. at (301) 796-6270.

Sincerely yours,

Christy L. Foreman -S

Christy Foreman, M.S.
Office Director
Office of Device Evaluation
Center for Devices and Radiological Health