Covidien LLC
Moshe J Cohen
Senior Regulatory Specialist
6135 Gunbarrel Ave
Boulder, Colorado 80301

March 4, 2024

Re: K230693
Trade/Device Name: BIS™ Advance Monitoring System
Regulation Number: 21 CFR 882.1400
Regulation Name: Electroencephalograph
Regulatory Class: Class II
Product Code: OLW, OMC, OLT, ORT

Dear Moshe J Cohen:

The Food and Drug Administration (FDA) is sending this letter to notify you of an administrative change related to your previous substantial equivalence (SE) determination letter dated February 26, 2024. Specifically, FDA is updating this SE letter due to incomplete contact name, which was incorrectly stated as Moshe Cohen as an administrative correction.

Please note that the 510(k) submission was not re-reviewed. For questions regarding this letter please contact Bradley Quinn, OHT1: Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices, 301-796-5575, bradley.quinn@fda.hhs.gov

Sincerely,

Bradley Q. Quinn -S

Bradley Quinn
Assistant Director
DHT1C: Division of Sleep Disordered Breathing, Respiratory and Anesthsia Devices
OHT1: Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

February 26, 2024

Covidien LLC
Moshe Cohen
Senior Regulatory Specialist
6135 Gunbarrel Ave
Boulder, Colorado 80301

Re: K230693
Trade/Device Name: BIS™ Advance Monitoring System
Regulation Number: 21 CFR 882.1400
Regulation Name: Electroencephalograph
Regulatory Class: Class II
Product Code: OLW, OMC, OLT, ORT
Dated: February 18, 2024
Received: February 20, 2024

Dear Moshe Cohen:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Bradley Q. Quinn -S

Bradley Quinn
Assistant Director
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K230693

Device Name
BIS™ Advance Monitoring System

Indications for Use *(Describe)*
The BIS™ Advance Monitoring System is intended for monitoring the state of the brain by data acquisition of EEG signals under the direct supervision of a licensed healthcare practitioner or by personnel trained in its proper use. The BIS™ Advance Monitoring System, and all its associated parameters, is intended for use on adults and pediatric patients (4 years old and above) within a hospital or medical facility.
For Adult patients, the BIS™ Index, one of the BIS™ Advance Monitoring System's output parameters, may be used to guide anesthetic administration of desflurane, isoflurane, propofol and sevoflurane with balanced anesthetic techniques in order to monitor the anesthetic effects on the brain.
The use of the BIS™ Index for monitoring may be associated with the following when used with propofol anesthesia: reduction in primary anesthetic use; reduction in emergence and recovery time; and reduction in incidence of awareness with recall.
For pediatric patients, ages 4 and above, the BIS™ Index, one of the BIS™ Advance Monitoring System's output parameters, may be used to guide anesthetic administration of sevoflurane with balanced anesthetic techniques in order to monitor the anesthetic effects on the brain.
The use of the BIS™ Index in pediatric patients, when used with sevoflurane anesthesia, has demonstrated a reduction in primary anesthetic use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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PRAStaff@fda.hhs.gov

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BIS™ Advance Monitoring System
510(k) Summary

This summary of 510(k) safety and effectiveness information for the BIS™ Advance Monitoring System is submitted in accordance with the Food and Drug Administration Rule to implement provisions of the Safe Medical Devices Act of 1990 and in conformance with the requirements of 21 CFR §807.92.

SUBMITTER INFORMATION

Submitted By:
Covidien, llc
6135 Gunbarrel Avenue
Boulder, CO 80301
Date Prepared: 09 March 2023
Contact Person:
Moshe J Cohen
Senior Regulatory Affairs Specialist
Phone: +972-507094475
Email: moshe.cohen2@medtronic.com

DEVICE

Trade Name: BIS™ Advance Monitoring System
Common Name: BIS™ Advance Monitoring System
Classification Regulation: 21 CFR 882.1400
Classification Name: Index-Generating Electroencephalograph Software
Regulatory Class: Class II
Primary Product Code: OLW
Secondary Product Code: OMC, OLT, ORT
Review Panel: Anesthesiology Devices

PREDICATE DEVICE

Predicate Manufacturer: Aspect Medical Systems, INC
Predicate Trade Name: BIS EEG Vista Monitor System and BISX
Predicate 510(k): K072286

PREVIOUS CORRESPONDENCE WITH FDA

Covidien held 2 Pre-Submission meetings with the FDA regarding this submission (Q200053 and Q200053_S001). Refer to VOL_020_Performance Testing Clinical for further details regarding previous correspondence with FDA.

DEVICE DESCRIPTION

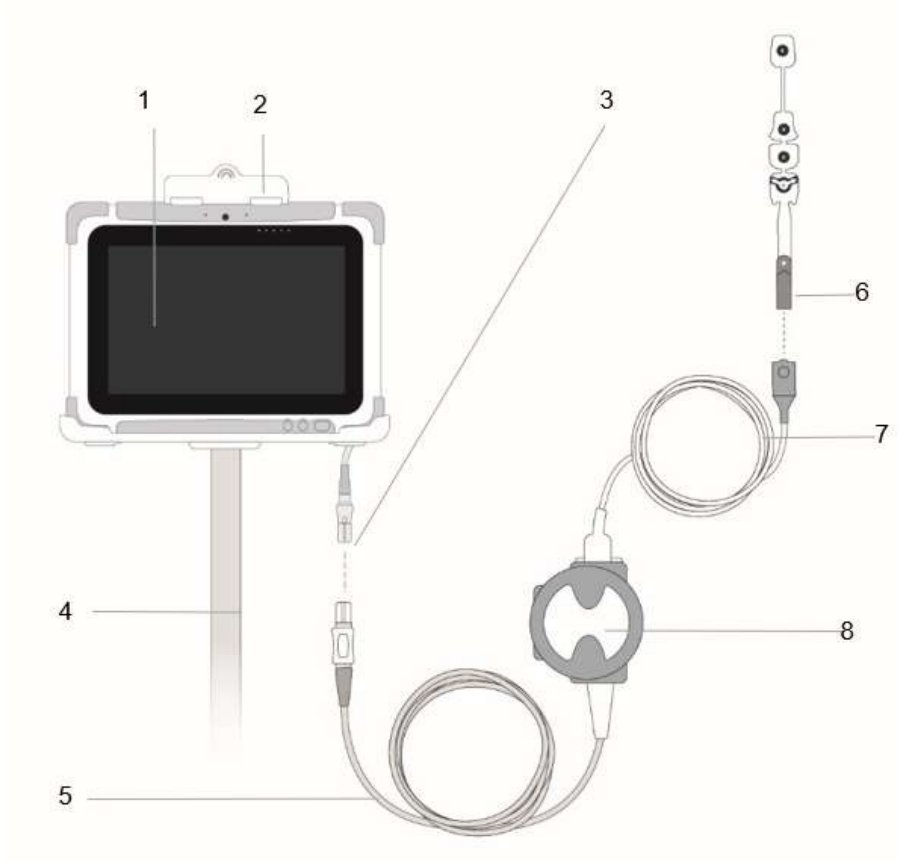
The BIS™ Advance Monitoring System is a user-configurable patient monitoring system designed to monitor the hypnotic state of the brain based on acquisition and processing of EEG signals. It processes raw EEG signals to produce a single number, called the Bispectral Index, or BIS value, which correlates with the patient's level of hypnosis.
The BIS™ Advance Monitoring system is comprised of the following components: BIS™ Advance Monitor, BIS™ Advance Docking Station, BIS™ Advance Adapter Cable, GCX Mounting Accessory, BISx/BISx4 Module, Patient Interface Cable (PIC) and Monitor Interface Cable (MIC).

The BIS™ Advance Monitor displays:

- The current BIS™ number
- Raw EEG waveforms in real time
- Various signal quality indicators (EMG, SQI)
- Trend graphs of processed EEG parameters (including various options)
- Processed EEG variables:
  - Electromyography (EMG)
  - Signal Quality Index (SQI)
  - Suppression Ratio (SR)
  - Burst Count (BURST) (for Extend Sensor and four-channel monitoring only)
  - Suppression Time (ST)
  - Spectral Edge Frequency (SEF)
  - Median Frequency (MF)
  - EEG Power Asymmetry Index (ASYM) (for four-channel monitoring only)
- Alarm Indicator and Messages

The BIS™ Advance Monitor displays 2 channels of EEG when connected to the BISx module and a unilateral BIS sensor (BIS™ Extend Sensor, BIS™ Pediatric Sensor and BIS™ Quatro Sensor) and displays 4 channels of EEG, two from each side of the brain, when connected to the BISx4 module and BIS™ Bilateral Sensor.
For both the 2-channel and the 4-channel systems, BIS monitoring is implemented as follows:
A sensor placed on the patient’s head transmits EEG signals to the BISx module. The BISx module filters the data, analyzes it for artifacts and processes it using digital signal processing techniques, then sends the data to the monitor for display. The purpose of processing the EEG waveform data is to extract characteristic features from the complex signal in order to provide easier pattern recognition of changes over time during the recording.

Figure 1. BIS™ Advance Monitoring System Components



Number	Component
1	BIS™ Advance Monitor
2	BIS™ Docking Station
3	BIS™ Adapter Cable
4	GCX mounting accessory
5	Monitor Interface Cable (MIC)
6	BIS™ Sensor
7	Patient Interface Cable (PIC)
8	BISx/BISx4 module

INDICATIONS FOR USE

The BIS™ Advance Monitoring System is intended for monitoring the state of the brain by data acquisition of EEG signals under the direct supervision of a licensed healthcare practitioner or by personnel trained in its proper use. The BIS™ Advance Monitoring System, and all its associated parameters, is intended for use on adults and pediatric patients (4 years old and above) within a hospital or medical facility.
For Adult patients, the BIS™ Index, one of the BIS™ Advance Monitoring System's output parameters, may be used to guide anesthetic administration of desflurane, isoflurane, propofol and sevoflurane with balanced anesthetic techniques in order to monitor the anesthetic effects on the brain.
The use of the BIS™ Index for monitoring may be associated with the following when used with propofol anesthesia: reduction in primary anesthetic use; reduction in emergence and recovery time; and reduction in incidence of awareness with recall.
For pediatric patients, ages 4 and above, the BIS™ Index, one of the BIS™ Advance Monitoring System's output parameters, may be used to guide anesthetic administration of sevoflurane with balanced anesthetic techniques in order to monitor the anesthetic effects on the brain.
The use of the BIS™ Index in pediatric patients, when used with sevoflurane anesthesia, has demonstrated a reduction in primary anesthetic use.

TECHNOLOGICAL CHARACTERISTICS COMPARISON

There are 2 proposed changes in this submission in regard to the predicate device. The first change is related to the indications for use, which will be narrowed down from the predicate device. The indications for use of the subject device now specify the minimum age of patients (4 years and above), as well as the specific anesthetic agents for which the BIS™ Advance Monitoring System may be utilized to guide administration of, and the clinical benefits that may be associated with when utilizing the BIS™ Advance Monitoring System to guide administration of specified anesthetic agents. The revised indications for use do not introduce any new indications, claims or target populations. The indication for use changes are supported by clinical studies and detailed in this submission in VOL_020_Performance Testing Clinical.
The second change is related to a new monitor design, the BIS™ Advance Monitor, which will replace the predicate monitor, the BIS VISTA Monitor. The BISx/BISx4 modules and the BIS™ Sensors are not modified as part of this submission and rely on the previously cleared 510k submissions, K072286 and K143506, respectively.
The BIS™ Advance Monitor is a customized off the shelf durable tablet designed for the same functionality as the predicate device, BIS VISTA Monitor: it displays EEG data and processed parameters computed by the BISx/BISx4 module either numerically and/or graphically, via user interface, and presents alarms when alarm thresholds are crossed. The new monitor is equipped with a larger display, additional user interface options and up-to-date operating system.

The BIS™ Advance Monitor is provided with a newly-developed software which integrates all key features of the predicate, while incorporating a user interface that closely mirrors it, along with minor changes and improvements, as summarized below:

- Display and user-interface modifications, to implement minor improvements and increased number of user-selection options
- New low-priority alarms and additional battery life alert
- Removal of two processed parameters, sEMG and sBIS, which have no clinical significance
- New electromagnetic interference artifact detection

The software change does not impact diagnosis and treatment, as no software changes were performed to the BISx/BISx4 module (the unit that performs the computation for EEG acquisition), the BIS algorithm nor to the algorithm database structure.
The change is mainly focused on the display of data while the principle of operation, main displayed parameters as well as the technology utilized for acquisition and processing of EEG waves are all unaffected by the change.
The verification and validation tests enable the use of the BIS™ Advance Monitor for use with the existing BISx/BISx4 module and the BIS™ sensors.
Based on the results of the verification and validation studies (including system verification), the subject device, the BIS™ Advance Monitor, is substantially equivalent to the predicate device.
The following technological characteristics comparison was performed on the BIS™ Advance Monitor of the subject device vs. the BIS Vista Monitor of the predicate device. The other components of both the subject and predicate devices are identical and will therefore be excluded from this comparison.

Table 1. Comparison of Technological Characteristics

Device Characteristic	**Subject Device** **BIS™ Advance Monitoring System**	**Predicate Device** **BIS EEG VISTA Monitor System and BISX (K072286)**	**Similarities and Differences**
Classification	II	II	Similar
Device Classification Name	Index-Generating Electroencephalograph Software	Index-Generating Electroencephalograph Software	Similar
Primary Product Code	OLW	OLW	Similar
Secondary Product Code(s)	OMC, OLT, ORT	OMC, OLT, ORT	Similar

Fundamental Technology	Acquisition, processing and display of real-time EEG waveforms and processed EEG parameters	Acquisition, processing and display of real-time EEG waveforms and processed EEG parameters	Similar
Principle of Operation	EEG signals are transmitted from sensors placed on patient's head to the BISx/BISx4 Module. The BISx module filters the data, analyzes it for artifact and processes it using digital signal processing techniques, then sends the data to the monitor for display.	EEG signals are transmitted from sensors placed on patient's head to the BISx/BISx4 Module. The BISx module filters the data, analyzes it for artifact and processes it using digital signal processing techniques, then sends the data to the monitor for display.	Similar
Regulation Number	882.1400	882.1400	Similar
Prescription/over the counter use	Prescription	Prescription	Similar
Intended Population	Adult and pediatric, from age 4 years and up	Adult and pediatric, without age limitation	Different: pediatric patients age is now limited
Intended Users	Professionally trained health care providers	Professionally trained health care providers	Similar
Environment of Use	hospitals or medical facilities providing patient care	hospitals or medical facilities providing patient care	Similar
Monitor	BIS™ Advance Monitor	BIS VISTA Monitor	Similar: Same functionality Different: minor software changes, mostly UI-related, SOUP and OS changes, updated hardware design,

			different dimensions and weight, new docking station, mounting accessories and adapter cable to connect to the monitor to the BISx/BISx4
Monitor – Primary External materials	Glass, TPR (Thermoplastic rubber), ABS (Acrylonitrile butadiene styrene), PC (Polycarbonate), Acrylic, Zinc alloy, Lexan 8B35 film	Glass, ABS (Acrylonitrile butadiene styrene), PC (Polycarbonate), Polyester, Polyutherane	Different (note - the monitor does not come in contact with the patient)
User interface	Default display options along with user-selection options for display of EEG and processed parameters and graphs; Display of alert messages; User-selection options for setting and configuring alarms	Default display options along with user-selection options for display of EEG and processed parameters and graphs; Display of alert messages; User-selection options for setting and configuring alarms	Similar: main features remain unchanged Different: More user-selection options compared to predicate, change to default settings for specific parameters, additional export-to-file support, new low-priority configurable alarms, additional battery life alert, minor

			display improvements
Electromagnetic interference artifact detection	Supported, system adjusts the Signal Quality Indicator accordingly	Not supported	Different: allows for a more accurate Signal Quality Indicator
Monitor Operating System	Windows 10 Enterprise	Windows CE	Different
Display size	Height: 5.3" Width: 8.5"	Height: 4" Width: 5.25"	Different
Module	BISX/BISX4	BISX/BISX4	Similar
Monitor accessories	Docking Station; GCX Clamp Mount / GCX Desktop Mount; Adapter Cable	Pole Clamp	Different: different monitor mounting accessories to accommodate the different monitor designs; New Adapter Cable to allow connection of the new monitor to the existing Monitor Interface Cable which connects to the BISx/BISx4 module
Sensors	BIS™ sensors (cleared under K143506): Quatro / Pediatric / Extend / Bilateral	BIS™ sensors (cleared under K143506): Quatro / Pediatric / Extend / Bilateral	Similar
Displayed data	EEG, BIS index, SR, ST, SQI, EMG, Burst Count, DSA, ASYM,	EEG, BIS index, SR, ST, SQI, EMG, Burst Count, DSA, ASYM, sEMG, sBIS,	Different: sEMG and sBIS removed

	artifact detection, alarm indicators and messages, trend graphs of processed EEG Parameters	artifact detection alarm indicators and messages, trend graphs of processed EEG Parameters	from subject device display due to not being supported by scientifically-proven clinical significance and device claims
Energy Source	AC-power source; Internal lithium-ion battery	AC-power source; Internal lithium-ion battery	Similar
Software level of concern	Moderate	Moderate	Similar
Sterility	Non-sterile	Non-sterile	Similar
Main Safety and Performance Standards	1. IEC 60601-1:2005+A1:2012 / ANSI/AAMI ES60601-1:2005/(R)2012 and A1:2012, C1:2009/(R)2012 and A2:2010/(R)2012 2. IEC 60601-1-2:2014 3. IEC 60601-1-6: 2010 +A1:2013 4. IEC 60601-1-8: 2006 + A1:2012 5. IEC 62366-1:2015 6. IEC 80601-2-26:2019 7. IEC 62133-2:2017	1. IEC 60601-1:2005+A1:2012+A2:2020 2. IEC 60601-1-2:2014+A1:2020 3. IEC 60601-1-6:2010 + A1:2013 +A2:2020 4. IEC 60601-1-8:2006 + A1:2012+A2:2020 5. IEC 62366-1:2015 + A1:2020 6. IEC 80601-2-26:2019 7. IEC 62133-2:2017	Similar, with the exception of 2020 amendments of several standards, which are still under transition period – the predicate device already complies with such amendments, while the subject device is scheduled to comply with the amendments before the end of the transition period

PERFORMANCE DATA
The following performance data is provided to support the substantial equivalence determination with the predicate device:

Electrical Safety and EMC
Electrical safety and EMC testing were performed per ANSI/AAMI ES 60601-1:2005/(R)2012 & A1:2012, C1:2009/(R)2012 & A2:2010/(R)2012, IEC 60601-1-2:2014. Additionally, testing was performed in accordance with the device-particular safety and performance standard, IEC 80601-2-26:2019.
Electrical Safety and EMC Test reports are provided in sections VOL_017_Electromagnetic Compatibility and Electrical Safety and VOL_018_ Performance Testing Bench.

General Performance
VOL_018_ Performance Testing Bench contains a summary of all the performance bench testing performed on the subject device.
The results of the bench performance testing demonstrate that the performance of the subject device, BIS™ Advance Monitor, complies with the requirements of testing standards applied.

Hazard/Risk Analysis
A hazard analysis was carried out on the BIS™ Advance Monitor's software in compliance with ISO 14971:2019. This hazard analysis concluded that any residual risks were judged as acceptable when weighed against the intended benefits of use of. The hazard analysis is detailed further in this submission in MISC FILES: 001_Extract of the monitor software-related items from BIS Advance Risk Management File.

Software
The software description and documentation, including test report, are provided in VOL_ 016_Software. The test report indicates that the BIS™ Advance Monitor software complies with all software requirements and design specifications.

Biocompatibility
The BIS™ Advance Monitor does not come into direct or in-direct contact with the patient. Therefore, no biocompatibility assessment is required.

Performance Testing - Animal
No animal performance testing was required to demonstrate subject device safety and effectiveness.

Performance Testing - Clinical

Clinical studies were performed and outlined in section VOL_020_Performance Testing Clinical of this submission. The proposed changes to the indications for use are supported via performance of the following clinical studies:

1. **Oliver (MDT19053OLIVER)**

This multicenter, prospective study was conducted to investigate the relationship between BIS™ and inhaled anesthetics across a wide range of anesthetic concentration and hypnotic states.
This study was conducted across 3 sites in the United States, in 143 subjects. Healthy volunteers were randomized to one of five anesthetic regimen groups: sevoflurane, sevoflurane with remifentanil, sevoflurane with fentanyl, desflurane, or isoflurane. The OLIVER trial determined the BIS50 and BIS95 values at which 50% and 95% of patients were unresponsive and found that these values were similar across all treatment groups BIS™ values were highly correlated with level of sedation and the prediction probabilities for correctly predicting whether a subject would respond to a verbal command were very high, suggesting that BIS™ is an excellent predictor for the level of consciousness.

2. **BTIGER (MDT20032BTIGER)**

This multicenter, prospective, randomized control study was conducted to investigate the relationship between BIS™ values including EEG profile and anesthetic agents in the pediatric population.
This study was conducted across 8 sites in the United States, in 170 subjects. Pediatric subjects aged 4 - 18 years (ASA PS I - III) undergoing routine sevoflurane general anesthesia were included in the trial. The BTIGER study determined the mean end-tidal sevoflurane (ETSevo) administration during the maintenance phase of anesthesia during pediatric surgery. ETSevo was statistically significantly lower in the BIS™ guided treatment group compared to the standard practice group. This study provides clinical evidence that the BIS™ index can be used to guide the anesthetic administration of sevoflurane in pediatric patients aged 4 – 18 years.

Previous Correspondence With FDA

Covidien held 2 Pre-Submission meeting with the FDA regarding this submission (Q200053_BIS and Q200053_S001_BIS). Refer to VOL_020_Performance Testing Clinical for further details regarding previous correspondence with FDA.

CONCLUSIONS

The subject device, BIS™ Advance Monitor is equivalent in intended use, technological characteristics and performance to the existing legally marketed predicate device. The subject device was tested to verify and validate the safety and performance of the new monitor and its substantial equivalence to the predicate device. From the evidence presented in this Premarket Notification, the subject device can be considered substantially equivalent to the predicate device.