November 13, 2019

Nox Medical
% John Smith
Partner
Hogan Lovells US, LLP
555 Thirteenth Street, NW
Washington, DC 20004

Re: K192469
Trade/Device Name: Nox Sleep System
Regulation Number: 21 CFR 882.1400
Regulation Name: Electroencephalograph
Regulatory Class: Class II
Product Code: OLZ, KZM
Dated: September 9, 2019
Received: September 9, 2019

Dear John Smith:

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,

Jay Gupta
Assistant Director
DHT5A: Division of Neurosurgical,
Neurointerventional
and Neurodiagnostic Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K192469

Device Name
Nox Sleep System

Indications for Use *(Describe)*
The Nox Sleep System is used as an aid in the diagnosis of different sleep disorders and for the assessment of sleep.

The Nox Sleep System is used to measure, record, display, organize, analyze, summarize, and retrieve physiological parameters during sleep and wake.

The Nox Sleep System allows the user to decide on the complexity of the study by varying the number and types of physiological signals measured.

The Nox Sleep System allows for generation of user/pre-defined reports based on subject´s data.

The user of the Nox Sleep System are medical professionals who have received training in the areas of hospital/clinical procedures, physiological monitoring of human subjects, or sleep disorder investigation.

The intended environments are hospitals, institutions, sleep centers, sleep clinics, or other test environments, including patient's home.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

nox medical

510(k) Summary

Submitter:	Nox Medical Katrinartuni 2 IS-105 Reykjavik Iceland Tel: +354 570 7170 Establishment Registration Number: 3007389703
Contact Person:	Kolbrun E Ottosdottir Chief Compliance Officer Katrinartuni 2 IS-105 Reykjavik Iceland
Application Correspondent:	John J. Smith, MD, JD Partner Hogan Lovells US LLP 555 Thirteenth Street, NW Washington, D.C. 20004
Preparation Date:	November 12, 2019
Device:	Device Proprietary Name: Nox Sleep System Device Common or Usual Name: Sleep Assessment System Classification Name: Electroencephalograph, Automatic Event Detection Software for Polysomnograph with Electroencephalograph Regulation Number: 882.1400 Product Code: OLZ, KZM Device Class: II Review Panel: Neurology
Predicate Devices:	Substantial equivalence is claimed to Compumedics Somté PSG System (K072201) from Compumedics Limited. The Nox T3 (K082113) from Nox Medical and Embletta MPR (K122516) from Embla Systems are used as reference devices.

Device Description

The Nox Sleep System is intended for patients undergoing physiological measurements, for the assessment of sleep quality and the screening for sleep disorders.

The Nox Sleep System does not provide any alarms and is not intended to be used for continuous monitoring where failure to operate can cause injuries or death of the patient.

The basic Nox Sleep System consists of two recording/acquisition devices (Nox A1 Recorder and Nox C1 Access Point), a software running on a PC (Noxturnal PSG), an Android application (Noxturnal App) running on mobile platform, along with sensors and accessories. The system supports full Polysomnography (PSG) studies both in ambulatory and online/attended setups but also more simple sleep study setups, recording only few channels. The ambulatory sleep studies may take place in the clinic or in the home environment, but the online/attended sleep studies are only conducted in the clinical environment.

The Nox A1 Recorder is a small battery-operated recording unit that is worn by the patient during the study. It records signals from patient applied sensors that connect to the unit but also supports recording of signals from auxiliary devices over Bluetooth. The Nox A1 Recorder allows for communication over Bluetooth with the Noxturnal App during ambulatory setup and with the Nox C1 Access Point during online setup. The recorder is intended to be worn over clothing.

New accessories and sensors as part of this submission are the Nox A1 EEG 5 Lead Gold Electrode Cable and Nox A1 EEG Head Cable that are used for recording of EEG/EOG. These components are in direct contact with the patient.

The Nox C1 Access Point is a separate mains powered unit located remotely from the patient that allows for recording of signals from auxiliary devices. It supports communication over LAN/Ethernet to the Noxturnal PSG, and communication with the Nox A1 Recorder and Noxturnal App over Bluetooth. The Nox C1 Access Point is only used for online study setup and is thus not intended to be used in the home environment.

The Noxturnal App is used as a mobile interface to the Nox A1 Recorder and Nox C1 Access Point. The communications are via Bluetooth link. The app is normally used in the beginning of a sleep study, for basic tasks such as device configuration, starting a recording, checking the signal quality of signals being recorded and marking events during bio calibration.

The Noxturnal PSG is used for configuration of the Nox recording/acquisition devices, to download a study from ambulatory recording or to collect an online study. The software supports the viewing, retrieving, storing and processing of data recorded/collected, manual and automatic analysis and reporting on the results from the recorded studies. The purpose with the automatic scoring function in Noxturnal PSG is to assist the trained physician in the diagnosis of a patient. It is not intended to provide the trained physician with a diagnostic results. The type of automatic analysis events scored by Noxturnal PSG include: Sleep Stages (Wake, N1, N2, N3, REM), Apneas, Hypopneas, Apnea Cassification (Obstructive, Mixed and Central Apneas), Limb Movements, Periodic Limb Movements, SpO2 Desaturation Events. and potential Bruxism-Related Events.

The result of the automatic analysis/scoring must always be manually verified by the trained physician prior to diagnosis.

Indication for Use

The Nox Sleep System is used as an aid in the diagnosis of different sleep disorders and for the assessment of sleep.

The Nox Sleep System is used to measure, record, display, organize, analyze, summarize, and retrieve physiological parameters during sleep and wake.

The Nox Sleep System allows the user to decide on the complexity of the study by varying the number and types of physiological signals measured.

The Nox Sleep System allows for generation of user/pre-defined reports based on subject´s data.

The user of the Nox Sleep System are medical professionals who have received training in the areas of hospital/clinical procedures, physiological monitoring of human subjects, or sleep disorder investigation.

The intended environments are hospitals, institutions, sleep centers, sleep clinics, or other test environments, including patient's home.

Technological Characteristics and Comparison

For the purpose of demonstrating substantially equivalency of the Nox Sleep System the Compumedics Somté PSG (K072201) System from Compumedics Limited has been selected as the primary predicate device.

Indication for Use*: "The Somté PSG is intended for use in the recording, displaying, analysis, printing and storage of human biological parameters such as heart and muscle activity, eye movement, breathing and body movements to assist in the diagnosis of various sleep disorders or sleep related respiratory or cardiac disorders. The Somté PSG is designed for ambulatory and mobile operation and can be used in either the patient's home, the hospital or other environments, thus enabling patients to be investigated under as realistic conditions as possible. The Somté PSG is only to be used under the direction of a physician. "*

The primary predicate Compumedics Somté PSG and the new device Nox Sleep System are both used for recording of physiological parameters of various origin to assist with diagnosis of sleep disorders/sleep related disorders and support the same types of sleep studies, i.e. full Polysomnography (PSG) studies both in ambulatory and online/attended setups but also more simple sleep study setups, recording only few channels. The intended environments and user groups are the same for both the primary predicate and the new device, and both devices are for prescription use only. The overall methodology relating to how the sleep studies are conducted and the recorded data displayed and analysed is also very similar for both the new device and the primary predicate.

It is thus concluded that the intended use of the Nox Sleep System may be regarded the same as that of the Compumedics Somté PSG System.

The comparison table below is provided as a summary of the most relevant characteristics of the Nox Sleep System relative to the primary predicate Compumedics Somté PSG.

Technological Characteristic	**Nox Sleep System**	**Compumedics Somté PSG System**	**Result of Comparison**
Portable design	Yes	Yes	Equivalent

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
Patient worn device	Yes	Yes	Substantially Equivalent
Physical dimensions	Nox A1 Recorder: 82x63x21 mm Nox C1 Access Point: 135x149x26 mm	Somté PSG Recorder: 113x65x30mm Patient input box: 53x133x25mm Bedside unit (dimensions not stated in labeling)	Substantially Equivalent The Embletta MPR (K122516) includes a separate device located remotely from the patient with very similar size 115x110x26mm
Weight	Nox A1 Recorder: 92 g (120 g with battery) Nox C1 Access Point: 264 g	Somté PSG Recorder: 110 g (172 g including batteries) Patient input box: 95 g Bedside unit (weight not stated in labeling)	Substantially Equivalent The Embletta MPR (K122516) includes a separate device located remotely from the patient with very similar weight 160g
Case Material	Plastic, ABS/Polycarbonate blend	Plastic, ABS/Polycarbonate blend	Equivalent
Method of Connection to Patient	Respiratory bands/belts for respiratory effort Respiratory bands/belts for attaching of device and clip straps to secure position of device Plastic tubing and cannula for pressure sensing Snap on electrode cables with snap-on disposable electrodes for EMG/EOG Thermal flow sensors/thermocouple for measuring of nasal/oral airflow Nox A1 EEG 5 Lead Gold Electrode Cable and Nox A1 EEG Head Cable for EEG/EOG **S**urface electrode leads for EEG/EOG/EMG Surface Electrodes for measuring of leg movements Wrist worn oximeter and probes for oximetry worn on finger	Respiratory bands/belts for respiratory effort Respiratory bands/belts for attaching of device and optional EZ Vest to secure position of device Plastic tubing and cannula for pressure sensing Snap on electrode cables with snap-on disposable electrodes for EMG/EOG Thermal flow sensors/thermocouple for measuring of nasal/oral airflow Surface electrode leads for EEG/EOG/EMG Surface Piezo Limb Sensor for measuring of leg movements Probes for oximetry worn on finger	Substantially Equivalent The use of an auxiliary 3rd party wireless oximeter that is wrist worn and connected via Bluteooth® to the recorder is substantially equivalent to Nox T3 (K082113).
Acquisition Units	Nox A1 Recorder Nox C1 Access Point	Somté PSG Recorder Patient Interface Box Bedside unit for recording of additional AUX channels	Substantially Equivalent Embletta MPR (K122516) includes a separate device allowing recording of auxiliary

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
			channels
Local User Interface	Nox A1 Recorder: Display (OLED), push buttons and indicator light on device Nox C1 Access Point: Light indicator on device, factory reset button Noxturnal App running on Android™ platform	Somté PSG Recorder: Display (LCD) and push buttons and indicator light on device	Substantially Equivalent The Noxturnal App is used in a very similar way as the display on the Somté PSG Recorder and may be regarded as an extension of the display screen on the Nox A1 Recorder.
Data Collection	Yes	Yes	Equivalent
Display Raw Data during Recording	Yes, By use of the Noxturnal PSG (PC) during in-lab use or by use of Noxturnal App	Yes, PC during in-lab use, or LCD on unit	Substantially Equivalent
Real-time waveforms preview	Yes – By use of the Noxturnal App including full disclosure waveform preview	Yes – Integrated LCD including full disclosure waveform preview	Substantilly Equivalent
Data display on PC for interpretation	Yes – during or after recording	Yes – during or after recording	Equivalent
Data Analysis	Yes - By use of Noxturnal PSG SW (PC application) Automatic, result may be manipulated (manual review/verification must be performed prior to diagnosis) Manual analysis Event marking (scoring) Technician Notes	Yes – By use of Profusion Sleep SW (PC application) Automatic, result may be manipulated (manual review/verification must be performed prior to diagnosis) Manual analysis Event marking (scoring) Technician Notes	Equivalent
Signal Sheets/Trace Display Layout properties – Adjust by user	Yes - By use of Noxturnal PSG SW (PC application) – such as: Timebase settings Signal grouping/arrangements Grid Markers Epoch Markers Apply changes to data type Background color Cursor color Grid color	Yes – By use of Profusion Sleep SW (PC application) – such as: Timebase settings Signal grouping/arrangements Grid Markers Epoch Markers Apply changes to data type Background color Cursor color Grid color	Equivalent
Signal trace properties – Adjust by user	Yes - By use of Noxturnal PSG SW (PC application) – such as: Select Input and reference Name Trace color	Yes – By use of Profusion Sleep SW (PC application) – such as: Select Input and reference Name Trace color	Equivalent

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
	Zoom Size Grids Polarity Upper/lower display bounds Filtering (HP/LP/Notch) Auto Scale Numeric Offset Adding/Deleting	Zoom Size Grids Polarity Upper/lower display bounds Filtering (HP/LP/Notch) Auto Scale Numeric Offset Adding/Deleting	
Display of graphical summary for selected traces and data for the entire study	Yes - By use of Noxturnal PSG SW (PC application)	Yes - By use of Profusion Sleep SW (PC application)	Equivalent
User defined event types	Yes - By use of Noxturnal PSG SW (PC application)	Yes - By use of Profusion Sleep SW (PC application)	Equivalent
Automatic Analysis/Detector Output for User Interpretation - per AASM recommendations/scoring rules	Yes - By use of Noxturnal SW (PC application) Sleep Stages: Wake, N1, N2, N3, REM Apneas, Hypopneas Classification of apneas: Obstructive, Mixed or Central Limb Movements, Periodic Limb Movements SpO2 desaturation events Potential Bruxism Related events	Yes - By use of Profusion Sleep SW (PC application) Sleep Stages: Wake, N1, N2, N3, REM Arousal detection and arousal classification Apneas, Hypopneas Classification of apneas: Obstructive, Mixed or Central Unsure respiratory event Limb Movements, Periodic Limb Movements Snores (detection from sound input baseline) Eye movements, singular, anti-phase and in-phase (EOG) SpO2 desaturation events and artifacts, min/max SpO2 values Potential Bruxism Related events Average position for each	Substantially Equivalent All automatic analysis provided in the new device is also provided in the primary predicate device. Relating to automatic analysis not included in the new device: The raw data necessary for the analysis of these events may be recorded and displayed in the Noxturnal PSG software for manual analysis

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
		epoch Average CPAP for each epoch Average TcCO2 value for each epoch Peak EtCO2 value of each respiratory cycle PTT event detection pH event detection	
Report Generation	Yes - By use of Noxturnal PSG SW (PC application)	Yes – By use of Profusion Sleep SW (PC application)	Equivalent
Statistics available for report fields	Statistics and graphs from manual scored events and automatic analysis	Statistics and graphs from manual scored events and automatic analysis	Equivalent
MSLT/MWT[1] studies supported	Yes	Yes	Equivalent
Data Inputs	Generic and custom sensors/auxiliary devices.	Generic and custom sensors/auxiliary devices.	Substantially Equivalent
Signal Conditioning	Yes	Yes	Substantially Equivalent
Remote Sleep Surveillance	Yes, via Ethernet	Yes, via Ethernet	Equivalent
Remote Capability to Monitor Lead Quality	Yes	Yes	Equivalent
Remote Capability to Monitor Recording Parameters	Yes	Yes	Equivalent
#Channels of data recorded	Nox A1 recorder Up to 26 Nox C1 Access Point Up to 16	Up to 25 + 8 (by use of Bedside station)	Substantially Equivalent No impact on use. Both devices have enough channels to select from to be able to perform full Polysomnography (PSG) sleep studies or a simpler Polygraphy (PG) studies.
Respiratory Effort Channels – Abdomen and Thorax	Yes	Yes	Equivalent
Airflow	Yes	Yes	Equivalent
Pressure	Yes	Yes	Equivalent
Snore	Yes	Yes	Equivalent
Respiratory sound/audio	Yes	Yes	Equivalent
Body position	Yes	Yes	Equivalent
SpO2	Yes	Yes	Equivalent
Pulse Rate	Yes	Yes	Equivalent

[1] Multiple Sleep Latency Test (MSLT), Maintenance of Wakefulness Test (MWT)

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
Plethysmograph/Pulse Waveform	Yes	Yes	Equivalent
Oximeter status (signal quality)	Yes	Yes	Equivalent
ECG	Yes	Yes	Equivalent
EEG	Yes	Yes	Equivalent
EOG	Yes	Yes	Equivalent
Submental/chin EMG	Yes	Yes	Equivalent
Leg Movement	Yes	Yes	Equivalent
Ambient light	Yes	Yes	Equivalent
Signals from Auxiliary Devices	Yes	Yes	Equivalent
Video	Yes	Yes	Equivalent
Impedance Check/Integrity Check	Yes - both	Yes - both	Equivalent
Power Source	Nox A1 Recorder: One 1.5 V AA battery Host PC via USB during data transfer Nox C1 Access Point: By use of medical power supply Nominal input: 100-240 V AC +/- 10%, 50-60 Hz, 0.350-0.150 Arms (at max load) Nominal output: 12 V DC +/- 5%, 0-1250 mA	2 x AA alkaline or NiMH batteries Bedside station (not stated in labeling)	Substantially Equivalent – Use of battery Powering by host PC via USB during data transfer is substantially equivalent to Nox T3 (K082113). Powering method of Nox C1 Access Point is substantially equivalent to Embletta MPR (K122516).
Communication Interface	Nox A1 Recorder: USB and Bluetooth® wireless technology Nox C1 Access Point: Ethernet and Bluetooth Wireless technology	Ethernet and Bluetooth® wireless technology	Equivalent – Ethernet and Bluetooth® wireless technology The USB communication interface is substantially equivalent to Nox T3 (K082113)
Recording time	Up to 8 hours	Up to 24 hours	Substantial Equivalent - No impact on use. 8 hours of recording is more than enough for sleep studies
Device Storage Media	Nox A1 Recorder: Internal Flash 1GByte	CF Card up to 2GByte	Substantially Equivalent No impact on use
Channel Sampling Rates	1 Hz-256 kHz channel dependent	1Hz -1024 Hz channel dependent	Substantially Equivalent No impact on use
Channel Storage Rate	1-200 Hz channel dependent	1-200 Hz channel dependent	Equivalent
Signal Processing	32 bit	16 bit	Substantially Equivalent No impact on use
Basic Safety and	IEC 60601-1	IEC 60601-1	Substantially Equivalent

Technological Characteristic	Nox Sleep System	Compumedics Somté PSG System	Result of Comparison
Essential Performance	IEC 60601-1-6 Nox A1 Recorder additionally IEC60601-1-11 IEC60601-2-25 IEC60601-2-26 IEC60601-2-40		
Electromagnetic Compatibility	IEC 60601-1-2	IEC 60601-1-2	Equivalent
Biocompatibility	Patient contacting components: Nox A1 EEG 5 Lead Gold Electrode Cable and Nox A1 EEG Head Cable Patient contacting materials: Riteflex, PVC, Santoprene and Gold Finished product has been tested according to ISO 10993-5 ISO 10993-10	Cleared as part of K072201	Substantially Equivalent

Performance Testing Summary

The Nox Sleep System was verified and validated throughout the design process according to requirement specifications, relevant standards and intended use to assure product safety, effectiveness, and reliability. Design and verification testing of all requirement specification defined for the Nox Sleep System was conducted. All labeling content was tested towards predefined labeling requirements considering, regulatory requirements, applicable product standards, labeling standards, and risk output. System level testing were conducted to verify configuration, communication, recording and storage capacity performance, safety, and reliability. All tests confirmed that the Nox Sleep System meets the predetermined acceptance criteria.

The Nox Sleep System has been evaluated and found be compliant to the following electromagnetic compatibility and electrical safety standards:

- IEC 60601-1 Medical electrical equipment - Part 1: General requirements for basic safety and essential performance
- IEC 60601-1-2 Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility - Requirements and tests

The Nox Sleep System has gone through assessment towards FDA's *"Information to Support a Claim of Electromagnetic Compatibility (EMC) of Electrically-Powered Medical Devices - Guidance for Industry and Food and Drug Administration Staff*". The conclusion of this design review is that the Nox Sleep System will function safely and effectively in its intended electromagnetic environment, including immunity to electromagnetic disturbance (interference), without introducing excessive electromagnetic disturbances (emissions) that might interfere with

other devices.

The Nox A1 Recorder along with patient applied sensors and components intended to be used in the patient's home during ambulatory studies have been evaluated and found to be compliant to the following electrical safety standard for home healthcare environment:

- IEC 60601-1-11 Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance – Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment

The Nox A1 Recorder, electrode leads and cables have been tested and found to be compliant to the following electrical safety standards:

- IEC 60601-2-25 Medical electrical equipment - Part 2-25: Particular requirements for the basic safety and essential performance of electrocardiographs,
- IEC 60601-2-26 Medical electrical equipment - Part 2-26: Particular requirements for the safety of electroencephalographs,
- IEC 60601-2-40 Medical electrical equipment - Part 2-40: Particular requirements for the safety of electromyographs and evoked response equipment

All body contacting components (Nox A1 EEG 5 Lead Gold Electrode Cable and Nox A1 EEG Head Cable) have gone through successful biocompatibility testing according to biocompatibility standards:

- ISO 10993-5 Third Edition 2009-06-01 Biological evaluation of medical devices – Part 5: Test for in vitro Cytotoxicity
- ISO 10993-10 Third Edition 2010-08-01 Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization.

Contact is characterized as Surface Contacting with intact skin for a limited (< 24 hour) duration in accordance with ISO 10993-1 and FDA's "*Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part; 1 Evaluation and testing within a risk management process*".

All Nox Sleep System lead wires and patient cable connectors are in compliance with "*21 CFR 898 - FDA Performance Standard for Electrode Lead Wires and Patient Cables* ".

Signals recorded by the Nox Sleep System underwent performance testing demonstrating that all the signal types being recorded comply with the performance criteria set forth by Nox Medical that includes the minimum performance specification recommended by the American Academy of Sleep Medicine (AASM)[2].

The signals recorded with the Nox Sleep System were compared to signals recorded with the primary predicate device Compumedics Somté PSG System. All signals required for the recording, scoring and reporting of standard Polygraphy and Polysomnography variables were present and displayed all expected changes in morphology during associated sleep and respiratory events. Furthermore, both systems showed the same characteristics over a standard clinically used timescale and were capable of adding, removing, re-referencing and filtering all signals as needed.

[2] Berry RB, Brooks R, Gamaldo CE et al. The AASM Manual for the Scoring of Sleep and Associated Events; Rules, Terminology and Technical Specifications

Both systems displayed all signals at a resolution necessary for complete sleep staging, ECG analysis and respiratory analysis. The conclusion from this comparison testing is that the method used for recording of physiological signals and the resulting signal waveforms displayed by the Nox Sleep System and the primary predicate Compumedics Somté PSG System may be deemed substantially equivalent.

The Nox Sleep System has undergone usability testing to comply with standard "*IEC 60601-1-6 Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - collateral standard: Usability*". The usability testing result was successful and did not raise new questions about safety or effectiveness. All usability goals are passed.

Nox Medical has implemented cybersecurity controls for the Nox Sleep System to assure the medical device cybersecurity and to maintain medical device functionality, safety, and effectiveness. Assessment was performed in accordance with FDA's "*Guidance for Industry - Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software*" and "*Content of Premarket Submissions for Management of Cybersecurity in Medical Devices*".

Software validation in accordance with FDA's "*General Principles of Software Validation; Final Guidance for Industry and FDA Staff* (January 11, 2002)" was conducted for the Nox Sleep System to ensure software specification conform to user needs and intended uses and that the particular requirements undertaken can be consistently fulfilled.

The Nox Sleep System has gone through assessment towards the FDA's *"Design Considerations for Devices Intended for Home Use - Guidance for Industry and Food and Drug Administration"*. The overall conclusion of this review is that the system is well designed and suited for its intended use in the home environment and meets the instructions set by this guidance.

The Nox Sleep System has gone through assessment towards the FDA's "*Radio Frequency Wireless Technology in Medical Devices - Guidance for Industry and Food and Drug Administration Staff*". Based on this guidance, the Nox Sleep System complies well with its instructions. Nox Medical has conducted wireless coexistence risk analysis and testing/evaluation according to the guidelines and FDA recognized consensus standards and telecommunication rules recommended in the agency's RF wireless technology guidance document.

The Nox Sleep System has undergone extensive benchtop performance testing to verify that the use of the Nox Sleep System in online and ambulatory setup delivers all configured signals for the entire duration of recordings and that no error occurs which would impact the intended use, and/or safety and efficiency of the system.

Design validation of the Nox Sleep System was conducted to demonstrate that the system is safe and effective for its intended use. The valiation testing conducted included both ambulatory and online recordings/setup and were run in a simulated clinical environment at Nox Medical, and in a home environment. The signals recorded were the gold standard signals used in polysomnography (PSG) to measure brain waves, respiration, and other signals during sleep for diagnostic of sleep disorders. The validation included standard clinical tasks including, but not limiting to hook up of patient, configuration of the devices, impedance check, bio calibration, review of real time data, analysis of data, view of reports, data downloading and review, and storage of data.

The non-clinical performance testing support the safety of the Nox Sleep System and the hardware and software verification and validation demonstrate that the Nox Sleep System should perform as intended in the specified use conditions. Based on the extensive performance bench

testing undertaken it may be concluded that the Nox Sleep System performs comparably with the predicate Compumedics Somté PSG System that is currently marketed for the same intended use and presents no new concerns about safety or effectiveness.

Clinical performance testing was conducted for the automatic scoring algorithms implemented in Nox Sleep System to demonstrate safety and effectiveness of the new device and to support substantial equivalence to the primary predicate Compumedics Somté PSG System. The clinical performance testing consisted of retrospectively analyzing pre-existing clinical data from sleep studies that had already been collected and manually scored as part of routine clinical care. All scorers were qualified polysomnographic technologists and followed the American Academy of Sleep Medicine (AASM) scoring guidelines. The study protocol consisted of exporting the reported indices/events from the pre-existing manual scoring and then running the automatic scoring algorithm in Noxturnal PSG on the same clinical data. The results of the automatic scoring were exported and compared to the results of the manually scored data. The overall conclusion of comparison of conditions of use and the clinical performance testing is that the Noxturnal PSG's automatic scoring tools are found to be acceptable as a scoring aid in the clinical routine and that the automatic function of the Nox Sleep System may perform comparably with those of the predicate Compumedics Somté PSG System that is currently marketed for the same intended use and presents no new concerns about safety or effectiveness. More details are given below for each automatic scoring algorithm:

Bruxism Analysis Summary*:*
The clinical purpose is to improve the efficiency of scoring EMG data that is consistent with potential bruxism-related events by labeling mandibular movements as measured by masseter EMG for review and confirmation by a trained healthcare professional.

Clinical data set/patient population: The automatic analysis was validated on adult Polygraphy recordings, including masseter EMG signal, recorded from multiple U.S. dental clinics collected as part of clinical routine.

	Sex	**Age [yrs]**	**Height [cm]**	**Weight [kg]**	**BMI**
Averages	Male 60% Female 40%	44.5 53	181.2 166.7	96.8 80.3	29.6 29.0

Justification: Due to the frequent occurrence of normal oromandibular movements during sleep the analysis was determined to be safe if it would reliable detect oromandibular movements, allowing the physician to review the analysis results and remove events which they determine to be normal. The safety endpoint was determined to be that the analysis would detect at least 90% of oromandibular movements considered by a human expert to be bruxism-related events with 95% confidence.

Result: The sensitivity of the analysis was 95.7% (95% CI 93.2% - 97.4%), specificity was 61.0% (95% CI 58.9% - 63.0%), PPV was 34.6% (95% CI 32.0% - 37.3%), NPV was 98.5% (95% CI 97.7% - 99.1%).

PLM Analysis Summary:
The clinical purpose is to improve the efficiency of scoring periodic limb movement events.

Clinical data set/patient population: The automatic analysis was validated on adult Polysomnography recordings recorded at a national hospital serving a general population who seeks medical attention at a sleep clinic.

Justification: The safety endpoint was defined to ensure interclass correlation of 0.61 or greater and a bias which is unlikely to impact a diagnosis

Result: The ICC for the Periodic Limb Movement Index was 0.87.

Respiratory Flow Analysis Summary (Cannula, RIP, calibrated RIP (cRIP))

1) AHI and ODI Algorithm Summary

The clinical purpose is to improve the efficiency of scoring Apneas, Hypopneas (using cannula, RIP or calibrated RIP (cRIP) signals) and desaturation events from oximeter.

Clinical data set/patient population: The automatic analysis was validated on adult Polysomnography recordings recorded at a national hospital serving a general population who seeks medical attention at a sleep clinic.

Justification: The analysis was determined to be safe if it met the safety endpoint of having a 95% confidence in not classifying patients with an AHI below 5 as having an AHI greater than or equal to 15 or having a 95% confidence in not classifying patients with an AHI greater than or equal to 15 as having an AHI below 5. Furthermore, the Cohen's kappa was reported.

Result: The Cohen's kappa for the Apnea Hypopnea Index (AHI) detection was 0.78 using a cannula, 0.62 (95% CI 0.59 – 0.66) using RIP flow, and 0.62 (95% CI 0.59 – 0.66) using cRIP flow. The Cohen's kappa for the Oxygen Desaturation Index (ODI) detection was 0.87.

Table 1 Contingency table for AHI scoring using cannula.

		AHI Automatic scoring			
		0-5	5-15	15-30	30+
AHI Manual scoring	0-5	76%	7%	0%	0%
	5-15	0%	9%	3%	0%
	15-30	0%	1%	3%	0%
	30+	0%	0%	1%	1%

Table 2 Contingency table for AHI scoring using RIP flow.

		AHI Automatic scoring			
		0-5	5-15	15-30	30+
AHI Manual scoring	0-5	65%	19%	0%	0%
	5-15	1%	7%	2%	0%
	15-30	0%	0%	4%	0%
	30+	0%	0%	1%	1%

Table 3 Contingency table for AHI scoring using cRIP flow.

		AHI Automatic scoring			
		0-5	5-15	15-30	30+
AHI Manual scoring	0-5	65%	18%	0%	0%
	5-15	2%	8%	3%	0%
	15-30	0%	0%	3%	1%
	30+	0%	0%	1%	1%

Table 4 Contingency table for ODI scoring.

		ODI Automatic scoring			
		0-5	5-15	15-30	30+
ODI Manual scoring	0-5	83%	3%	0%	0%
	5-15	0%	8%	1%	0%
	15-30	0%	1%	3%	0%
	30+	0%	0%	0%	0%

2) Apnea Classification Algorithm Summary:

The clinical purpose is to improve the efficiency of classifying apneas into central apneas, mixed apneas or neither.

Clinical data set/patient population: The automatic analysis was validated on adult Polygraphy recordings recorded at a national hospital serving a general population who seeks medical attention at a sleep clinic.

Justification: The acceptance criteria was an ICC comparable to what has been reported in scientific literature of Central Apnea Index 0.46.

Result: The ICC was 0.91 and Cohen's kappa was 0.89 for the Central Apnea Index.

Sleep Staging Analysis Summary:

The clinical purpose is to improve the efficiency of scoring sleep stages with the intent of estimating total sleep time.

The following events are scored: Sleep stage W (Wake), Stage N1, Stage N2, Stage N3 and Stage R (REM).

Clinical data set/patient population: The automatic analysis was validated on adult recordings recorded at a national hospital serving a general population who seeks medical attention at a sleep clinic.

Justification: To measure total sleep time with 10% error or less assuming 80% sleep efficiency, results in the required accuracy of wake detection of 60% or better. The safety endpoint was determined to be an average accuracy of at least 60% when scoring wake epochs.

Results: The Cohen's Kappa was calculated resulting in κ=0.67. The results of the stage-by-stage ICC comparison are shown in Table 5. The accuracy of predicting the sleep stages resulted in N1 (9.8%), N2 (87.0%), N3 (83.0%), Wake (66.7%) and REM (82.5%).

Table 5 Confusion matrix comparing the classification of sleep stages with manual and automatic scoring.

		Automatic Analysis						
		W	N1	N2	N3	REM	Unassigned	Epoch Count
Manual Staging	W	**66.7%**	3.4%	19.8%	3.6%	6.3%	0.2%	2,207
	N1	22.5%	**9.8%**	46.6%	0.7%	20.3%	0.2%	2,032
	N2	1.5%	1.6%	**87.0%**	7.2%	2.5%	0.3%	11,560
	N3	0.3%	0.1%	16.1%	**83.0%**	0.3%	0.3%	4,838
	REM	2.6%	1.0%	12.6%	0.7%	**82.5%**	0.7%	4,557

Conclusion

Based on the comparison to the predicate devices, and extensive safety and performance testing, it is the conclusion of Nox Medical that the Nox Sleep System is substantially equivalent to the currently U.S. legally marketed device Compumedics Somté PSG System (K072201) and presents no new concerns about safety or effectiveness.