January 7, 2022

inomed Medizintechnik GmbH
Tomasz Moszkowski, PhD
Product Manager IOM
Im Hausgruen 29
Emmendingen, 79312
Germany

Re: K212166
Trade/Device Name: ISIS Headboxes and ISIS Neurostimulator
(ISIS IOM Systems: ISIS Xpert®, ISIS Xpert®Plus, ISIS Xpress)
Regulation Number: 21 CFR 882.1870
Regulation Name: Evoked Response Electrical Stimulator
Regulatory Class: Class II
Product Code: GWF
Dated: December 2, 2021
Received: December 6, 2021

Dear Alexander Maier:

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,

for
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)*

Device Name
ISIS Headboxes and ISIS Neurostimulator
(ISIS IOM Systems: ISIS Xpert®, ISIS Xpert®Plus, ISIS Xpress)

Indications for Use *(Describe)*
ISIS Headbox 5042xx products:

The products are intended for intraoperative neuromonitoring; for recording of electrophysiological signals and stimulating of nerve and muscle tissues.

The products are intended for use in the operating room to measure and display the electrical signals generated by muscle, peripheral nerves and the central nervous system. The products support the clinical application of Electroencephalography (EEG), Electromyography (EMG), Somatosensory Evoked Potentials (SEP), Motor Evoked Potentials (MEP), and Auditory Evoked Potentials (AEP).

The products are not intended for monitoring life-sustaining functions.

ISIS Neurostimulator 504180:

The ISIS Neurostimulator is intended for provision of neurophysiological stimulation when used in surgical procedures and for diagnostics. It is suitable for continuous operation and can be used in the following fields:
– Transcranial electrical stimulation (TES)
– Direct cortical stimulation (DCS)
– Direct nerve stimulation (DNS)
– Transcutaneous electrical nerve stimulation (TNS)
– Direct muscle stimulation (DMS)

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."

510(k) Summary

Submission Date:	07 July 2021
510(k) Holder:	inomed Medizintechnik GmbH Im Hausgrün 29 79312 Emmendingen, Germany
Submitter and Application Correspondent:	Tomasz Moszkowski, Ph.D. Phone: +49 7641 6414 583 Email: t.moszkowski@inomed.com
Manufacturing Site:	inomed Medizintechnik GmbH Im Hausgrün 29 79312 Emmendingen, Germany
Trade Name:	ISIS Headboxes and ISIS Neurostimulator (ISIS IOM Systems: ISIS Xpert®, ISIS Xpert®Plus, ISIS Xpress)
Common and Classification Name:	Evoked response stimulator and intraoperative monitor
Classification Regulation:	Primary: 21 CFR §882.1870 Secondary: 21 CFR §882.1400, 21 CFR §882.1375, 21 CFR §882.1900
Product Code:	GWF
Subsequent Product Codes:	GWJ, GWQ, ETN, IKN
Regulation Medical Specialty:	Neurology

Substantially Equivalent Devices:

	Predicate 510(k) Number	Predicate Manufacturer/ Model
Predicate Device:	K162199	Cadwell Industries Inc./ Cascade IOMAX Intraoperative Monitor

Device Description:

The ISIS Headboxes and the ISIS Neurostimulator constitute multimodality intraoperative neuromonitoring systems called ISIS IOM Systems. These systems consist of custom stimulation and recording hardware, a standard laptop or desktop personal computer running an off-the-shelf operating system, and operating software called NeuroExplorer. As an option, these systems mount on device carriers or housings tailored for intraoperative use.

The ISIS IOM Systems support the following measurement modalities:

- Auditory Evoked Potentials
- Transcranial and cortical Motor Evoked Potentials
- Somatosensory Evoked Potentials
- Freerunning and triggered Electromyography
- Electroencephalography
- Train of Four

Intended Use and Indications for Use:

ISIS Headbox 5042XX:

The products are intended for intraoperative neuromonitoring; for the recording of electrophysiological signals and stimulating nerve and muscle tissues.

The products are intended for use in the operating room to measure and display the electrical signals generated by muscle, peripheral nerves, and the central nervous system. The products support the clinical application of Electroencephalography (EEG), Electromyography (EMG), Somatosensory Evoked Potentials (SEP), Motor Evoked Potentials (MEP), and Auditory Evoked Potentials (AEP).

The products are not intended for monitoring life-sustaining functions.

The members of the ISIS Headbox 5042XX family and their indications for use are listed as follows:

Table 1: Product-specific indications for the use of the ISIS Headbox 5042XX medical product family

Product	Indications
504285 ISIS Headbox 8 Ch. DIF – 8 Ch. REF – AEP	EEG, SSEP, AEP, EMG, MEP
504281 ISIS Headbox 16Ch. REF-AEP	EEG, SSEP, AEP
504271 ISIS Headbox 16 Ch. DIF	EMG, MEP
504261 ISIS Headbox 16Ch. REF	EEG, SSEP

ISIS Neurostimulator 504180:

The ISIS Neurostimulator is intended for the provision of neurophysiological stimulation when used in surgical procedures and for diagnostics. It is suitable for continuous operation and can be used in the following fields:

- Transcranial electrical stimulation (TES)
- Direct cortical stimulation (DCS)
- Direct nerve stimulation (DNS)
- Transcutaneous electrical nerve stimulation (TNS)
- Direct muscle stimulation (DMS)

Comparison of Intended Use and Indications for Use:

The ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) are equivalent in terms of intended use and indications for use to the predicate device. Compared to the predicate device, the subject device is not intended for measuring visually evoked potentials (VEP), galvanic skin response, heart rate, and oxygen saturation (SpO_2). These differences, however, do not result in deteriorated clinical performance of the subject device in terms of its intended use nor do they raise questions in terms of safety. The current performance corresponds to the state of the art and adheres to up-to-date guidelines of intraoperative neuromonitoring.

	Subject devices	Predicate device	Claimed Equivalence
System	ISIS Headbox 5042XX and ISIS Neurostimulator	Cascade IOMAX	-
Manufacturer	inomed Medizintechnik GmbH	Cadwell Industries, Inc.	-
Picture			-

510(k) Number	K212166	K162199	-
Device Class	II	II	Equal
Product Code	GWF	GWF	Equal
Subsequent Product Codes	GWJ, GWQ, ETN, IKN	DQA, ETN, GWE, GWJ, GWQ, GZO, IKN, JXE, OLT	GWJ – Equal GWQ – Equal ETN – Equal IKN – Equal GWE, DQA, GZO, JXE, OLT are not within the scope of the intended use and indications for the use of the ISIS Headbox and ISIS Neurostimulator
Main function, site of usage, intended user group			
Main function	ISIS Headboxes 5042XX: "The products are intended for use in the operating room to measure and display the electrical signals generated by muscle, peripheral nerves and the central nervous system."	"The Cascade IOMAX™ Intraoperative Monitor with Surgical Studio software (IOMAX) is an electroneurodiagnostic device that acquires, displays and stores physiologic data from peripheral sensory and motor nerves, muscles and the central nervous system, generated either spontaneously or elicited by well-defined stimuli."	Equal Both the predicate and subject devices can acquire, display and store physiologic data from peripheral nerves, muscles and the central nervous system.
Site of usage	ISIS Headboxes 5042XX: "The products are intended for intraoperative neuromonitoring" "The products are intended for use in the operating room (…)"	"IOMAX is used (...) in a professional healthcare facility environment for pre-operative, intraoperative and post-operative testing."	Equivalent The predicate and the subject device are intended for intraoperative testing. The Cadwell IOMAX may in addition be used for pre-operative and post-operative monitoring, which the subject device is not intended for. This difference is clearly stated within the intended use statement of the subject device and thus does not raise questions in terms of product safety and effectiveness.
Intended user group	Neurophysiologists (clinical neurophysiologists, neurosurgeons, neurologists or medical technical assistants for functional diagnostics)	"IOMAX is used by or under the direction of a licensed physician, surgeon, or neurologist (…)"	Equivalent Both the predicate and subject devices may be used by licensed physicians (the ISIS Headbox intended use statement specifies the

			physicians to persons with clinical neurophysiologic background and medical technical assistants) and neurologists. Also, both the predicate and subject devices may be used by surgeons. The notion is more specifically stated within the documentation of the ISIS Headbox, i.e., it restricts the use to neurosurgeons that are licensed neurophysiologists.
Indended Use and Indications for Use			
Intended use	ISIS Headbox 5042XX: "The products are intended for intraoperative neuromonitoring; for the recording of electrophysiological signals and stimulating of nerve and muscle tissues. (…)" ISIS Neurostimulator 504180: "The ISIS Neurostimulator is intended for the provision of neurophysiological stimulation when used in surgical procedures and for diagnostics. (…)"	"The Cascade IOMAX™ Intraoperative Monitor with Surgical Studio software (IOMAX) is an electroneurodiagnostic device that acquires, displays and stores physiologic data from peripheral sensory and motor nerves, muscles and the central nervous system, generated either spontaneously or elicited by well-defined stimuli. (…) The system also delivers direct nerve stimulation required for specific surgical procedures."	Equal Both the subject and predicate device are intended for the recording of electrophysiological signals and stimulation of nerve and muscle tissues during intraoperative neuromonitoring.
Indications for use	ISIS Headbox 5042XX: "The products support the clinical application of (…) Auditory Evoked Potentials (AEP) (…)" ISIS Neurostimulator 504180: The ISIS Neurostimulator is intended for the provision of neurophysiological stimulation (…). It is suitable for continuous operation and can be used in the following fields: - Transcranial electrical stimulation (TES)	"Evoked Potentials (Eps): IOMAX provides electrical, auditory or visual stimulation (…). "	Equivalent Both the subject and predicate device are intended for provision of electrical and auditory stimulation. The ISIS Headbox 504281 and 504285 incorporate an AEP stimulator. The ISIS Neurostimulator is intended to be used for different modes of electrical stimulation. The modes of electrical stimulation in the ISIS Neurostimulator are described in more detail with regard to TES, DCS, DNS, TNS, and DMS than within the statement of Cadwell IOMAX. This is only a

	- Direct cortical stimulation (DCS) - Direct nerve stimulation (DNS) - Transcutaneous electrical nerve stimulation (TNS) - Direct muscle stimulation (DMS)		difference in the formulation of the statement and it does not raise questions in terms of device safety and effectiveness. The subject device is not intended for VEP stimulation and recording.
	ISIS Headbox 5042XX: "The products support the clinical application of Electroencephalography (EEG)"	"EEG: IOMAX measures, displays, records, and stores electrical activity of the brain from two or more electrodes on the head."	Equal Both the subject and predicate devices are intended for electroencephalography (EEG).
	ISIS Headbox 5042XX: "The products support the clinical application of (…) Electromyography (EMG)."	"Free Run EMG: IOMAX acquires, displays, records, and stores spontaneous EMG activity of motor nerves by continually displaying a live stream of mechanically induced myotome contractions."	Equal Both the subject and predicate devices are intended for electromyography (EMG).
	ISIS Headbox 5042XX: "The products support the clinical application of (…) Motor Evoked Potentials (MEP)." ISIS Neurostimulator 504180: "It is suitable for continuous operation and can be used in the following fields: (…) transcranial electrical stimulation (TES)."	"TcMEP: IOMAX delivers transcranial stimulation via dedicated outputs for intraoperative assessment."	Equal Both devices are capable of delivering transcranial stimulation via dedicated outputs. The ISIS Headbox is capable of recording MEP signals during transcranial electrical stimulation provided by the ISIS Neurostimulator.
	ISIS Neurostimulator 504180: "It is suitable for continuous operation and can be used in the following fields: (…) direct cortical stimulation (DCS)."	"Cortical Stimulation: IOMAX delivers Low Current Stimulation (LCS) during surgical procedures to map various areas of the cortex."	Equal Both devices are capable of delivering electrical current for direct cortical stimulation.
	ISIS Headbox 5042XX: "The products support the clinical application of (…) Electromyography (EMG)." ISIS Neurostimulator 504180: "It is suitable for continuous operation and can be used in the following fields: (…) direct nerve stimulation (DNS)."	"Triggered EMG (TEMG): IOMAX electrically stimulates the motor nerves, and displays, records, and stores the resulting compound muscle action potentials in the innervated muscle."	Equal Both devices are capable of measuring triggered EMG signals. The subject devices achieve this by combining the EMG measurement using the ISIS Headboxes and direct nerve stimulation (DNS) using the ISIS Neurostimulator.

	ISIS Headbox 5042XX: "The products are intended for use in the operating room to measure and display the electrical signals generated by muscle, peripheral nerves and the central nervous system." ISIS Neurostimulator 504180: "The ISIS Neurostimulator is intended for the provision of neurophysiological stimulation (…) in the following fields: (…) Direct nerve stimulation (DNS)."	"Nerve Conduction Study (NCS): IOMAX measures, displays, records, and stores sensory and motor nerve conduction time (latency) by applying a stimulus to peripheral nerves, the spinal cord, and the central nervous system."	Equivalent Both devices can be used to apply stimuli to the peripheral nerves and to the central nervous system. The subject device is capable of measuring, displaying and storing electrical signals generated by peripheral nerves (for which the nerve conduction velocity is normally measured). The subject device can also measure the latency and latency differences between evoked potentials from different sources. This difference can be used to calculate the nerve conduction velocity. The calculated result is, however, not directly stored. This difference does not pose any questions in terms of safety and performance, because the user can still perform the nerve conduction velocity measurement and document the results within the patient report via manual comment input.
	ISIS Headboxes 5042XX: "The products support the clinical application of (…) Electromyography (EMG)." ISIS Neurostimulator 504180: "The ISIS Neurostimulator is intended for the provision of neurophysiological stimulation (…) in the following fields: (…) transcutaneous electrical nerve stimulation (TNS)."	"Train of Four (TOF) or Twitch Test: IOMAX delivers a train of four pulses and measures, displays, records, and stores the compound muscle action potential amplitude fade for analysis."	Equal Both products can be used for performing twitch tests in order to measure the level of muscle relaxation due to muscular blockers. This measurement is performed by employing a simultaneous transcutaneous electrical nerve stimulation and EMG measurement. Although the indications for use statement of the subject device does not explicitly refer to the TOF measurement, the modality is available within the device design (software) and the product labelling. This difference in the formulation of the indications for use

			statement does not pose any questions in terms of safety and performance.
	ISIS Headbox 5042XX: "The products are not intended for monitoring life-sustaining functions."	"SpO2: IOMAX measures and displays oxygen saturation and heart rate information. Remote Reader: IOMAX provides passive, real time remote review of intraoperative monitoring for a physician outside of the operating room."	Not applicable The subject device is not intended for measuring and displaying oxygen saturation and heart rate. Vital parameter measurement is out of scope of the subject device. SpO2 and heart rate measurements are one of several physiological parameters that are normally tracked by anesthesia and available for IONM personnel to consider when interpreting neurophysiologic signals. The IONM guidelines published up to date do not specify the SpO2 monitoring as a required component of neurophysiologic monitoring systems (MacDonald et al., 2013, 2019; Nuwer et al., 2012; Sutter et al., 2007; Tyner, FS., 1994).

Technology Comparison:

The ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) and the predicate device are equivalent in terms of the technological characteristics. Among others, the technological differences exist predominantly within the technology used for signal recording and electrical stimulation.

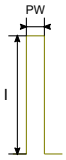
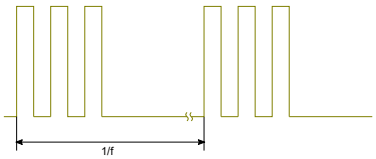
The subject device can acquire physiological signals with a sampling rate and bandwidth lower than the predicate devices but using a higher number of recording channels. The differences in the recording technology do not raise questions in terms of performance because both the subject and predicate device employ oversampling and are capable of measuring signals within the clinically relevant bandwidth.

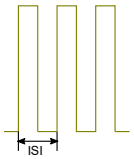
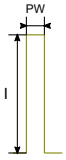
The stimulator of the subject device can deliver more energy than the predicate device, which results from the subject device being able to supply longer stimulation pulses or pulses at a higher frequency than the predicate. This is although the predicate can provide a higher current intensity in TcMEP mode than the subject device. This difference does not raise questions in terms of safety of the subject

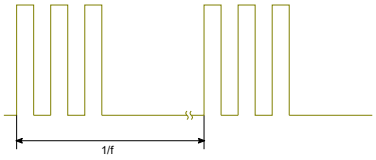
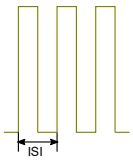
device because the resulting current densities for the cleared accessories are equivalent to those of the predicate device. Moreover, clinical performance is assured because the performance specifications of the predicate and subject devices fall within the wide range of stimulation parameters, pulse widths and intensities that are employed by well-established clinical methods to elicit physiological responses relevant for intraoperative neuromonitoring.

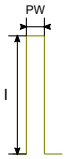
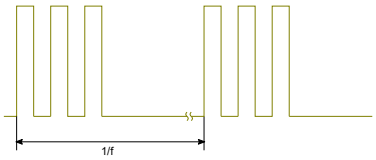
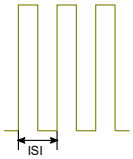
The technological differences do not raise questions in terms of safety and effectiveness of the device and are substantially equivalent for the use of the device for intraoperative neuromonitoring.

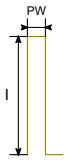
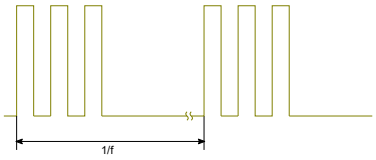
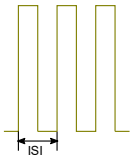
<table>
<tr><th></th><th>Subject device</th><th>Predicate device</th></tr>
<tr><td>System</td><td>ISIS Headbox 5042XX and ISIS Neurostimulator</td><td>Cascade IOMAX</td></tr>
<tr><td>Manufacturer</td><td>inomed Medizintechnik GmbH</td><td>Cadwell Industries, Inc.</td></tr>
<tr><td colspan="3">Technical aspects</td></tr>
<tr><td>Protection against electrical shock</td><td>Class I protection</td><td>Class I protection</td></tr>
<tr><td>Protection against electrical shock of patient leads</td><td>Device type BF (Body Floating)</td><td>Device type BF (Body Floating)</td></tr>
<tr><td>System configuration</td><td>Computer-based equipment with dedicated hardware and software components</td><td>Computer-based equipment with dedicated hardware and software components</td></tr>
<tr><td colspan="3">Signal recording</td></tr>
<tr><td>Measurement principle</td><td>Amplifiers based on differential (bipolar) and referential (unipolar) type of recording</td><td>Amplifiers based on differential (bipolar) and referential (unipolar) type of recording</td></tr>
<tr><td>Amplifier components</td><td>Desired combination of ISIS Headboxes with a total of 64 channels</td><td>One (1) Cortical Module
Up to four (4) Limb Modules</td></tr>
<tr><td>Number of amplifier channels</td><td>Up to 64:
<table>
<tr><th>Module</th><th>Channels</th></tr>
<tr><td>ISIS Headbox 16 Ch. REF (504261)</td><td>Unipolar: 16
Bipolar: 0</td></tr>
<tr><td>ISIS Headbox 16 Ch. DIF (504271)</td><td>Unipolar: 0
Bipolar: 16</td></tr>
<tr><td>ISIS Headbox 16 Ch. REF – AEP (504281)</td><td>Unipolar: 16
Bipolar: 0</td></tr>
<tr><td>ISIS Headbox 8 Ch. DIF – 8 Ch. REF – AEP (504285)</td><td>Unipolar: 8
Bipolar: 8</td></tr>
</table></td><td>Up to 48:
<table>
<tr><th>Module</th><th>Channels</th></tr>
<tr><td>Cortical Module</td><td>Unipolar: 13
Bipolar: 3</td></tr>
<tr><td>Limb Module</td><td>Unipolar: 0
Bipolar: 8</td></tr>
</table></td></tr>
</table>

A/D resolution	16-bit	16-bit
Hardware bandpass	Hardware high-pass filter: 0.5-120 Hz on all modules Hardware low-pass filter: 2500, 5000 Hz on all modules	Hardware high-pass filter: 0.3-100 Hz on cortical module 0.5-100 Hz on limb module Hardware low-pass filter: 30-5000 Hz on cortical module 30-10000 Hz on limb module
Sampling frequency	20 kHz	25 kHz
Notch filter	50, 60 Hz	50, 60 Hz
Common-mode rejection ratio (CMRR)	> 100 dB Conformant with IEC 80601-2-26:2019, clause 201.12.1.106 Common mode rejection.	> 115 dB Conformant with IEC 60601-2-26:2012, clause 201.12.1.101.5 Common mode rejection
Amplifier noise	Conformant with IEC 80601-2-26:2019, clause 201.12.1.104 Input noise	Conformant with IEC 60601-2-26:2012, clause 201.12.1.101.3 Input noise
Stimulation		
TcMEP stimulation	Realized by High Current Stimulator (HC) in transcranial stimulation mode	Realized by Cortical Module in TcMEP mode
Stimulator type	Current controlled	Current controlled and optional voltage controlled
No. of outputs	12	9
Stimulation intensity (I) and pulse width (PW)		
	Current controlled: up to 250 mA (voltage limit of 410 V) Voltage controlled: n/a 0.05 – 2 ms	Current controlled: up to 1500 mA (voltage limit of 1000 V) Voltage controlled: up to 1000 V 0.05 – 0.5 ms
Intensity step	Constant current: 0.1 mA Constant voltage: n/a	Constant current: 10 mA Constant voltage: 5 V
No. of stimulus pulses	1-9	1-9
Stimulation frequency (f) range		
	Up to 500 Hz	Up to 1 Hz

Limitation of stimulation frequency	1/10 pulse width to stimulation period ratio	None
Limitation of inter-stimulus interval		
	Limited to ½ pulse width to ISI	Minimum ISI: 0.1 ms
Absolute minimum inter-stimulus interval	0.1 ms	0.1 ms
Maximum charge per phase	189.66 µC	750 µC
Maximum RMS stimulation intensity	30 mA RMS	7.1 mA RMS
Minimum electrode size	0.39 cm²	Low EP: 0.04 cm² TcMEP: 0.5 cm
Maximum current density	76.92 mA/cm²	Low EP: 90.8 mA/cm² TcMEP: 14.1 mA/cm2
Maximum charge density	61.5 µC/cm²	Low EP: 275 µC/cm² TcMEP: 100 µC/cm²
Maximum power density	160 W/cm²	Low EP: 10 W/cm² TcMEP: 2,000 W/cm²
Power limitation	≤50 mJ/pulse Conformant to IEC 60601-2-40:2016, clause 201.12.4.103.	≤50 mJ/pulse IEC 60601-2-40:1998 (1st ed.), clause 201.12.4.103.
High-current stimulator for SEP and TOF	Realized by High Current Stimulator (HC) in subcutaneous stimulation (SEP, TOF) mode	Realized by Limb Module in High EP mode
Stimulator type	Constant current	Constant current
No. of outputs	12	5
Stimulation intensity (I)		
	Up to 75 mA	Up to 100 mA
Intensity step	0.1 mA	0.5 mA

Pulse width (PW)	0.05 – 2 ms	0.05 – 1 ms
No. of stimulus pulses	1-9	1
Stimulation frequency (f) range		
	SEP: Up to 500 Hz TOF: 2 Hz (fixed)	Up to 50 Hz
Limitation of stimulation frequency	1/10 pulse width to stimulation period ratio	None
Limitation of inter-stimulus interval		
	Limited to ½ pulse width to ISI	n/a (only 1 pulse possible)
Absolute minimum inter-stimulus interval	0.1 ms	n/a (only 1 pulse possible)
Maximum charge per phase	150 µC	100 µC
Maximum RMS stimulation intensity	23.7 mA RMS	Low EP: 3.6 mA High EP: 3.2 mA
Minimum electrode size	0.272 cm²	Low EP: 0.04 cm² High EP: 0.5 cm
Maximum current density	87.1 mA/cm²	Low EP: 90.8 mA/cm² High EP: 6.4 mA/cm²
Maximum charge density	150.0 µC/cm²	Low EP: 275 µC/cm² High EP: -
Maximum power density	20.7 W/cm²	Low EP: 10 W/cm² High EP: -
Power limitation	≤50 mJ/pulse Conformant to IEC 60601-2-40:2016, clause 201.12.4.103.	≤50 mJ/pulse IEC 60601-2-40:1998 (1st ed.), clause 201.12.4.103.
Low-current stimulator for direct cortical stimulation:	Realized by High Current Stimulator (HC) in direct cortical stimulation mode	Realized by Cortical Module in Low EP mode

Stimulator type	Constant current	Constant current
Stimulation intensity (I)		
	Up to 30 mA	Up to 20 mA
Intensity step	0.01 mA	0.01 mA
Pulse width (PW)	0.05 – 2 ms	0.05 – 1 ms
No. of stimulus pulses	1 – 9	1
Stimulation frequency (f) range		
	Up to 500 Hz	Up to 50 Hz
Limitation of stimulation frequency	1/10 pulse width to stimulation period ratio	None
Limitation of inter-stimulus interval		
	Limited to ½ pulse width to ISI	n/a (only 1 pulse possible)
Absolute minimum inter-stimulus interval	0.1 ms	n/a (only 1 pulse possible)
Maximum charge per pulse	60 µC	20 µC
Maximum RMS stimulation intensity	9.5 mA RMS	3.6 mA RMS
Minimum electrode size	0.126 cm²	Low EP: 0.04 cm²
Maximum current density	75.29 mA/cm²	Low EP: 90.8 mA/cm²
Maximum charge density	150.8 µC/cm²	Low EP: 275 µC/cm²
Maximum power density	7.1 W/cm²	Low EP: 10 W/cm²

Power limitation	≤50 mJ/pulse Conformant to IEC 60601-2-40:2016, clause 201.12.4.103.	≤50 mJ/pulse IEC 60601-2-40:1998 (1st ed.), clause 201.12.4.103.
Low-current stimulator for direct nerve stimulation:	Realized by Direct Nerve Stimulator (DNS) in direct nerve stimulation mode	Realized by Cortical Module in Low EP mode
Stimulator type	Constant current	Constant current
No. of outputs	1	1 + 1 (optional)
Stimulation intensity (I)		
	Up to 5 mA	Up to 20 mA
Intensity step	0.01 mA	0.01 mA
Pulse width (PW)	0.05 – 2 ms	0.05 – 1 ms
No. of stimulus pulses	1 – 9	1
Stimulation frequency (f) range		
	Up to 500 Hz	Up to 50 Hz
Limitation of stimulation frequency	1/10 pulse width to stimulation period ratio	None
Limitation of inter-stimulus interval		
	Limited to ½ pulse width to ISI	n/a (only 1 pulse possible)
Absolute minimum inter-stimulus interval	0.1 ms	n/a (only 1 pulse possible)
Maximum charge per pulse	10 µC	20 µC
Maximum RMS stimulation intensity	1.58 mA RMS	3.6 mA RMS

Minimum electrode size	0.020 cm²	Low EP: 0.04 cm²
Maximum current density	79 mA/cm²	Low EP: 90.8 mA/cm²
Maximum charge density	158 µC/cm²	Low EP: 275 µC/cm²
Maximum power density	1.25 W/cm²	Low EP: 10 W/cm²
Power limitation	≤50 mJ/pulse Conformant to IEC 60601-2-40:2016, clause 201.12.4.103.	≤50 mJ/pulse IEC 60601-2-40:1998 (1st ed.), clause 201.12.4.103.

Summary of Performance Testing:

Biocompatibility: The ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) have no patient contact materials, and therefore this section does not apply.

Software: The inomed NeuroExplorer Software is a MODERATE level of concern software. The software was designed and developed according to a rigorous development process, including software verification and validation. Software information is provided in accordance with internal requirements and the following guidance documents and standards:

- FDA guidance: The content of premarket submissions for software contained in medical devices, May 11, 2005
- FDA guidance: Off-the-shelf software use in medical devices, Sep 27, 2019
- FDA guidance: General principles of software validation: Final guidance for industry and FDA staff, Jan 02, 2002
- FDA guidance: Content of premarket submissions for management of cybersecurity in medical devices, Oct 02, 2014
- IEC 62304:2006, Medical device software – Software life cycle processes

Test results demonstrate that the inomed NeuroExplorer Software complies with its predetermined specifications, the applicable guidance documents, and standards.

Electrical Safety: The ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) were tested according to the following standards:

- IEC 60601-1:2005 (Third Edition) + CORR. 1:2006 + CORR. 2:2007 + A1:2012 (or IEC 60601-1: 2012 reprint), Medical electrical equipment – Part 1: General requirements for basic safety and essential performance.
- IEC 80601-2-26:2019, Medical electrical equipments – Part 2-26: Particular requirements for the basic safety and essential performance of electroencephalographs
- IEC 60601-2-40:2016, Medical electrical equipments – Part 2-40: Particular requirements for the basic safety and essential performance of electromyographs and evoked response equipment

Test results demonstrate that the products comply with the applicable standards.

Electromagnetic Compatibility:

The ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) were tested according to the following standards:

- IEC 60601-1-2:2014, Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral standard: Electromagnetic disturbances – Requirements and tests.

Test results demonstrate that the products comply with the applicable standards.

Performance Testing – Bench

The essential performance and safety of the ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) were tested for performance in accordance with internal requirements. The devices including their accessories and corresponding intended combinations with further products have been designed according to requirement specifications formulated at the following levels:

- Requirements for electrical medical systems
- Requirements for the system carrier
- Requirements for the amplifier (ISIS Headboxes) and stimulator (ISIS Neurostimulator) modules
- Requirements for the operating software (NeuroExplorer) incl. ISIS Headbox and ISIS Neurostimulator firmware
- ISIS Headbox and ISIS Neurostimulator accessories (adaptor boxes)
- Custom Microsoft® Windows 10 image

The products successfully underwent the bench testing to confirm the fulfillment of the requirements at these levels as part of the verification and validation process.

Moreover, the testing of the influence of human factors on the devices demonstrates that the products are safe to use and that no further improvement of the user interface design relating to safety is necessary.

The non-clinical tests demonstrate that the device is as safe, as effective, and performs as well as or better than the legally marketed device predicate.

Performance Testing – Clinical

No additional clinical testing was performed for the ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress). Therefore, this section does not apply.

Conclusion

In order to establish the performance and safety characteristics, the ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) underwent successful testing in terms of the device software, electrical safety, electromagnetic compatibility, bench testing, and human factors engineering. The results of these activities demonstrate that the devices are as safe, effective and perform as well as or better than the predicate device.

Therefore, the ISIS Headboxes and ISIS Neurostimulator including accessories as part of ISIS IOM Systems (ISIS Xpert®Plus, ISIS Xpert®, ISIS Xpress) are considered substantially equivalent to the predicate device.