

K112881

510(k) Summary

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Submitter: Nexstim Oy
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Manufacturing Site: Nexstim Oy
Elimaenkatu 9b
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Trade Name: Nexstim Navigational Brain Stimulation (NBS) System 4, and
Nexstim NBS System 4 with NEXSPEECH®

Classification Name: Stimulator, electrical, evoked response

Classification Regulation: 21 CFR §882.1870, 21 CFR §882.4560, 21 CFR §890.1375

Product Code: GWF, HAW, IKN

Substantially Equivalent Devices:	<i>New Nexstim Model</i>	<i>Predicate 510(k) Number</i>	<i>Predicate Manufacturer / Model</i>
	Nexstim Navigational Brain Stimulation (NBS) System 4	K091457	Nexstim Oy / eXimia Navigated Brain Stimulation System
	Nexstim NBS System 4 with NEXSPEECH®	K924226	Radionics, Inc. / Ojemann Cortical Stimulator
		K091457	Nexstim Oy / eXimia NBS System

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Device Description: The NBS System 4 combines magnetic resonance imaging-based, three dimensional localization of cortical motor areas of the brain with non-invasive TMS and simultaneous electromyography measurement to locate areas of the brain that are capable of evoking muscle responses when stimulated.

NEXSPEECH[®] is intended to be used in conjunction with the NBS System 4 for localization and assessment of cortical areas of speech function for pre-procedural planning purposes.

Indications for Use: The Nexstim Navigated Brain Stimulation System (NBS System) 4 is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System 4 provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning.

Nexstim NEXSPEECH[®], when used together with the Nexstim NBS System 4, is indicated for noninvasive localization of cortical areas that do not contain essential speech function. Nexstim NEXSPEECH[®] provides information that may be used in pre-surgical planning in patients undergoing brain surgery. Intraoperatively, the localization information provided by NEXSPEECH[®] is intended to be verified by direct cortical stimulation.

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] are not intended to be used during a surgical procedure. The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] are intended to be used by trained clinical professionals.

Technology Comparison: The Nexstim NBS System and NBS System with NEXSPEECH[®] employ the same technological characteristics as the predicate devices.

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Summary of Performance Testing:

Biocompatibility

Patient contact materials which are part of the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] were designed to comply with the following standard:

- *ISO 10993-1: 2009, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process,*

and were determined to be safe to use with patients.

Software Verification and Validation

Software for the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] was designed and developed according to a robust software development process, and were rigorously verified and validated.

Software information is provided in accordance with internal documentation and the following Standards and guidance documents:

- *FDA guidance: The content of premarket submissions for software contained in medical devices, 11 May 05;*
- *FDA guidance: Off-the-shelf software use in medical devices, 09 Sep 99;*
- *FDA guidance: General principles of software validation; Final guidance for industry and FDA staff, 11 Jan 02;*
- *IEC 60601-1-4: 2000, Medical electrical equipment Medical electrical equipment – Part 1-4: General requirements for safety – Collateral Standard: Programmable electrical medical systems; and*
- *IEC 62304: 2006, Medical device software – Software life cycle processes.*

Test results indicate that the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] comply with its predetermined specifications, and the Standards and guidance documents.

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Electrical Safety

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] were tested for performance in accordance with the following Standards:

- *IEC 60601-1: 1988, Am1: 1991, Am2: 1995, Medical electrical equipment - Part 1: General requirements for safety;*
- *IEC 60601-1-1: 2000, Medical electrical equipment – Part 1-1: General requirements for safety – Collateral standard: Safety requirements for medical electrical systems;*
- *IEC 60950-1: 2005, Information technology equipment – Safety – Part 1: General requirements; and*
- *UL 2601-1: 1997, Medical electrical equipment - Part 1: General requirements for safety.*

Test results indicated that the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] comply with the Standards.

Electromagnetic Compatibility (EMC) Testing

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] was tested for performance in accordance with the following Standard:

- *IEC 60601-1-2: 2007, Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral standard: Electromagnetic compatibility – Requirements and tests.*

Test results indicated that the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] comply with the Standards.

Performance Testing – Bench

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] were tested for performance in accordance with internal documentation and the following FDA Guidance Documents and Standards:

- *Guidance for Industry and Food and Drug Administration Staff Class II Special Controls Guidance Document: Repetitive Transcranial Magnetic Stimulation (rTMS) Systems; and*
- *IEC 60601-2-40:1998, Medical electrical equipment - Part 2-40: Particular requirements for the safety of electromyographs and evoked response equipment.*

Test results indicated that the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH[®] comply with its predetermined specification and the applicable Standard.

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Performance Testing – Usability

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® were tested for usability in accordance with the following Standards:

- *IEC 60601-1-6: 2010, Medical electrical equipment – Part 1-6: General requirements for basic safety and essential performance – Collateral standard: Usability; and*
- *IEC 62366: 2007, Medical devices – Application of usability engineering to medical devices.*

Test results indicated that the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® comply with the applicable Standards.

Performance Testing – Clinical

The clinical performance of the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® was established by literature review and appropriate clinical study and validation testing.

The test results indicated that the Nexstim NBS System 4 is safe and effective for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. Furthermore, the test results indicated that the Nexstim NBS System 4 with NEXSPEECH® is safe and effective for noninvasive localization of cortical areas that do not contain essential speech function.

NEXSPEECH® Clinical Study Description

Nexstim has conducted a clinical trial to assess the safety and to establish the effectiveness of Nexstim Navigated Brain Stimulation (NBS) System with NEXSPEECH when used for preoperative mapping of essential language cortex that could be at risk during a surgical procedure. As the gold standard for intraoperative language mapping, direct cortical stimulation (DCS) performed during an awake surgery was selected as the reference method for the comparison (Tharin, Golby 2007). In the study, the mapping results obtained using Nexstim NBS System with NEXSPEECH module were compared to those obtained by invasive DCS performed during awake surgery.

Preoperative speech mapping with NEXSPEECH was performed utilizing an object naming task time-locked to a rapid-rate transcranial magnetic stimulation train to non-invasively create a transient virtual lesion and thereby identify essential language areas (Lioumis 2012). Intraoperative language mapping was performed utilizing an object naming task and a simultaneous direct electrical stimulation of the exposed cortex to identify essential language areas (Picht 2006). The DCS was performed according to the normal clinical practice used at each study site.

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Subject Population

Speech mapping with Nexstim NBS with NEXSPEECH and intraoperative cortical stimulation was performed in 20 patients (age 25-70, 10 females) with a lesion requiring surgical intervention in the vicinity of essential language areas recruited at departments of neurosurgery at 2 university hospitals.

Comparison to Reference Method

The locations of areas relevant to speech production were determined prior to surgery non-invasively with Nexstim NBS System and NEXSPEECH. The patients were subsequently operated by a neurosurgeon that performed a language mapping with DCS during an awake surgery procedure.

Locations with positive or negative language response during direct cortical stimulation in the awake surgery were compared to those found in mapping with Nexstim NBS and NEXSPEECH module. A quantitative and qualitative analysis was carried out to evaluate the concordance of results obtained with both methods.

Localization Assessment

In order to evaluate the anatomical location of stimulation effects, each individual brain was divided into 37 individually named anatomical regions (Corina 2010). The NBS data and intraoperative DCS mapping data were both projected on the brain surface divided in this manner. See Figure 1 for schematic representation of the anatomical areas.

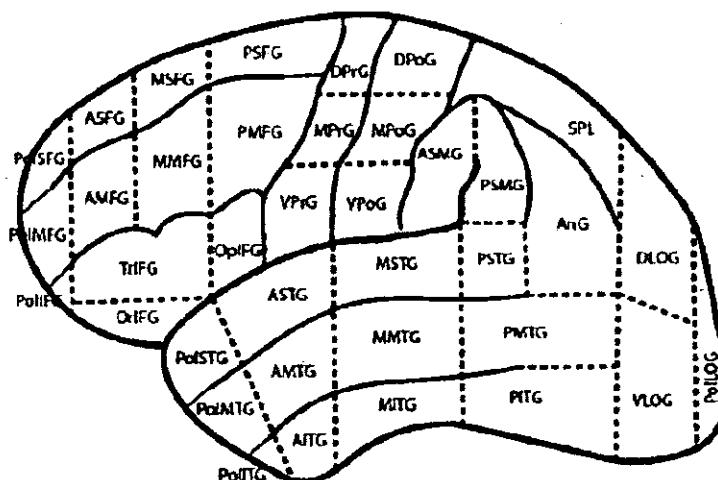


Figure 1. Schematic representation of the anatomical areas used for assessing concordance of speech area localization by NBS NEXSPEECH and DCS.

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NexSpeech® Clinical Study Conclusions

Safety

No adverse events related to NEXSPEECH use were reported in the patient population.

Effectiveness

The results of the present clinical trial demonstrate that NEXSPEECH has high sensitivity but relatively low specificity for localizing language areas. NEXSPEECH mapping has a very high overall negative predictive value everywhere in the brain (NPV=0.84), and particularly so in classical Broca (NPV = 1.0)

Due to the high sensitivity of NEXSPEECH in obtaining speech responses, negative responses obtained with NEXSPEECH can be used to identify brain regions where DCS responses are unlikely to be obtained. This information on negative speech locations can be utilized for planning procedures. With this strategy, any positive NEXSPEECH responses should be verified by intraoperative DCS.

Nexstim concludes that the clinical performance of NEXSPEECH speech mapping is sufficient for noninvasive localization of cortical areas that do not contain essential speech function. Intraoperatively, the localization information provided by NEXSPEECH® should be verified by direct cortical stimulation.

References

Corina DP, Loudermilk BC, Detwiler L, Martin RF, Brinkley JF, Ojemann G. Analysis of naming errors during cortical stimulation mapping: implications for models of language representation. *Brain Lang.* 2010 Nov;115(2):101-12.

Lioumis P, Zhdanov A, Mäkelä N, Lehtinen H, Wilenius J, Neuvonen T, Hannula H, Deletis V, Picht T, Mäkelä JP. A novel approach for documenting naming errors induced by navigated transcranial magnetic stimulation. *J Neurosci Methods.* 2012 Mar 15;204(2):349-54.

Picht, T., Kombos, T., Gramm, H.J., Brock, M., Suess, O., 2006. Multimodal protocol for awake craniotomy in language cortex tumour surgery. *Acta Neurochir (Wien)* 148, 127-137; discussion 137-128.

Tharin S and Golby A. Functional brain mapping and its applications to neurosurgery. *Neurosurgery* 60:185-201, 2007

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Conclusion

Verification and validation activities were conducted to establish the performance and safety characteristics of the Nexstim NBS System 4 and Nexstim NBS System 4 with NEXSPEECH®. The results of these activities demonstrate that the Nexstim NBS System 4 and Nexstim NBS System 4 with NEXSPEECH® is safe and effective when used in accordance with its intended use and labeling.

Therefore, the Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® are considered substantially equivalent to the predicate device.

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Comparison of Device Specifications – NBS System 4

<i>Characteristic</i>	<i>Nexstim Oy eXimia NBS System (K091457)</i>	<i>Nexstim Oy NBS System 4</i>
<i>Intended use</i>	The Nexstim eXimia Navigated Brain Stimulation System (NBS System) is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning. The NBS System is not intended to be used during a surgical procedure. The NBS System is intended to be used by trained clinical professionals.	The Nexstim Navigated Brain Stimulation System (NBS System) is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning. The Nexstim NBS System is not intended to be used during a surgical procedure. The Nexstim NBS System is intended to be used by trained clinical professionals.
<i>Tracking system accuracy</i>	1.6 mm (mean error in localization of the tool)	1.6 mm (mean error in localization of the tool)
<i>Navigation principle</i>	Based on anatomy (MRI picture) and calculated electric field	Based on anatomy (MRI picture) and calculated electric field
<i>TMS stimulus mode</i>	Single pulse	Single pulse
<i>Coil configuration</i>	Figure 8-shaped focal coil	Figure 8-shape focal and cooled focal coils
<i>Maximum applicator surface temperature</i>	Focal coil: 41 °C	Focal coil: 41 °C Cooled focal coil: 43 °C.
<i>Stimulation Output</i>	Maximum electric field ~150 Volts/meter (V/m) measured 25 mm below the coil.	Maximum electric field ~172 V/m measured 25 mm below the coil.
<i>Maximum output in motor threshold (MT) units</i>	~2.2 times the motor threshold (MT) of a healthy adult hand muscle where 1 MT corresponds to 45% stimulation intensity.	~2.5 times the MT of a healthy adult hand muscle where 1 MT corresponds to 40% stimulation intensity.
<i>Current waveform</i>	Biphasic	Biphasic
<i>Pulse length</i>	~280 µs	~230 µs
<i>Trigger input/output</i>	5V TTL input and output	5V TTL output
<i>EMG assessment</i>	Muscle response to stimulation measured with eXimia EMG	Muscle response to stimulation measured with eXimia EMG
<i>Number of EMG channels</i>	Up to 6 channels	Up to 6 channels
<i>EMG measurement range</i>	10 - 500 Hz	10 - 500 Hz
<i>Sampling rate</i>	3 kHz	3 kHz

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Comparison of Device Specifications – NBS System 4		
Characteristic	Nexstim Oy eXimia NBS System (K091457)	Nexstim Oy NBS System 4
<i>Common mode rejection ratio (CMRR)</i>	> 90 dB at 10 - 250 Hz	> 90 dB at 10 - 250 Hz
<i>NBS system with TMS electrical rating</i>	Voltage: 100 - 120 Vac 220 - 240 Vac Frequency: 50/60 Hz	Voltage: 100 - 120 Vac 220 - 240 Vac Frequency: 50/60 Hz
<i>EMG electrical rating</i>	Voltage: 120 - 240 Vac Frequency: 50/60 Hz	Voltage: 120 - 240 Vac Frequency: 50/60 Hz
<i>Weight</i>	eXimia weight: 300 kg TMS weight: 140kg Floor stand: 60kg	Total weight: 223 kg NBS System 4 has TMS II stimulator housed in the same cart with the whole NBS system.
<i>Dimensions</i>	TMS cabinet: 72 cm (width) x 60 cm (depth) x 98 cm (height) NBS System cart: 80 cm (width) x 70 cm (depth) x 120 cm (height)	All housed in the NBS System 4 cart: 80 cm (width) x 70 cm (depth) x 209 cm (max. height)

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Comparison of Device Specifications - Nexstim NBS System 4 with NEXSPEECH®			
Characteristic	Nexstim Oy eXimia Navigated Brain Stimulation System (K091457)	Integra Radionics Inc. Ojemann Cortical Stimulator (K924226)	Nexstim Oy NBS System 4 with NEXSPEECH®
<i>Intended use</i>	<p>The Nexstim eXimia Navigated Brain Stimulation System (NBS System) is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning.</p> <p>The NBS System is not intended to be used during a surgical procedure.</p> <p>The NBS System is intended to be used by trained clinical professionals.</p>	<p>Intended for intraoperative cortical stimulation mapping to aid in cortical resections in the vicinity of essential cortex.</p> <p>Motor mapping: locate sensorimotor cortex and descending motor pathways to identify the safest corridor to the tumour. Confirm anatomic integrity of the motor pathways during and after tumour resection.</p> <p>Speech mapping: identify essential language sites to maximise the extent of the tumour resection and minimise permanent language deficits.</p>	<p>Nexstim NEXSPEECH®, when used together with the Nexstim NBS System, is indicated for noninvasive localization of cortical areas that do not contain essential speech function. Nexstim NEXSPEECH® provides information that may be used in pre-surgical planning in patients undergoing brain surgery. Intraoperatively, the localization information provided by NEXSPEECH® is intended to be verified by direct cortical stimulation.</p> <p>The Nexstim NBS System with NEXSPEECH is not intended to be used during a surgical procedure.</p> <p>The Nexstim NBS System with NEXSPEECH is intended to be used by trained clinical professionals.</p>
<i>Area of brain to be stimulated</i>	Motor cortex	Essential cortex. Sensorimotor cortex and descending motor pathways. Essential language sites.	Language areas
<i>Stimulation response detection</i>	Response to stimulation measured with eXimia EMG	Muscle response measured with external/3 rd Party EMG. Response qualified by Clinician in real time	Response to stimulation measured with eXimia EMG for MT determination. Response qualified by clinician in real time with regard to a response to speech area stimulation, and additional video/audio recording for full off-line review.
<i>rTMS mode supported</i>	No	Yes	Yes
<i>rTMS frequency range</i>	Manually triggered single pulses (no rTMS)	Frequency selectable from 5, 10, 20, 50, 57 and 100Hz	0,1-10 Hz in 0,1 Hz steps



Food and Drug Administration
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Nexstim Oy
c/o Mr. Rainer Harjunpää
Director of Quality and Regulatory Affairs
Elimäenkatu 9B, FI-00510
Helsinki, Finland

MAY 22 2012

Re: K112881

Trade/Device Name: Nexstim Navigated Brain Stimulation (NBS) System 4, Nexstim NBS System 4 with NEXSPEECH (TM)
Regulation Number: 21 CFR 882.1870
Regulation Name: Evoked Response Electrical Stimulator
Regulatory Class: Class II
Product Code: GWF, HAW, IKN
Dated: May 3, 2012
Received: May 10, 2012

Dear Mr. Harjunpää:

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. 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.

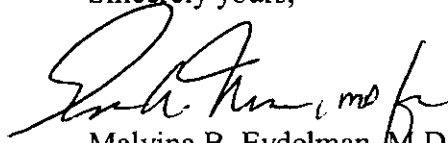
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to <http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm> for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,



Malvina B. Eydelman, M.D.

Director

Division of Ophthalmic, Neurological,
and Ear, Nose and Throat Devices

Office of Device Evaluation

Center for Devices and

Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K112881

Device Name: Nexstim Navigated Brain Stimulation (NBS) System 4 and NBS System 4 with NEXSPEECH®

Indications for Use: The Nexstim Navigated Brain Stimulation System (NBS System) 4 is indicated for non-invasive mapping of the primary motor cortex of the brain to its cortical gyrus. The NBS System 4 provides information that may be used in the assessment of the primary motor cortex for pre-procedural planning.

Nexstim NEXSPEECH®, when used together with the Nexstim NBS System 4, is indicated for noninvasive localization of cortical areas that do not contain essential speech function. Nexstim NEXSPEECH® provides information that may be used in pre-surgical planning in patients undergoing brain surgery. Intraoperatively, the localization information provided by NEXSPEECH® is intended to be verified by direct cortical stimulation.

The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® are not intended to be used during a surgical procedure. The Nexstim NBS System 4 and NBS System 4 with NEXSPEECH® are intended to be used by trained clinical professionals.

Prescription Use X
(Part 21 CFR 801 Subpart D)

AND/OR Over-The-Counter Use _____
(21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

KRISTEN BOWSHER
(Division Sign-Off)
Division of Ophthalmic, Neurological and Ear,
Nose and Throat Devices

510(k) Number K112881