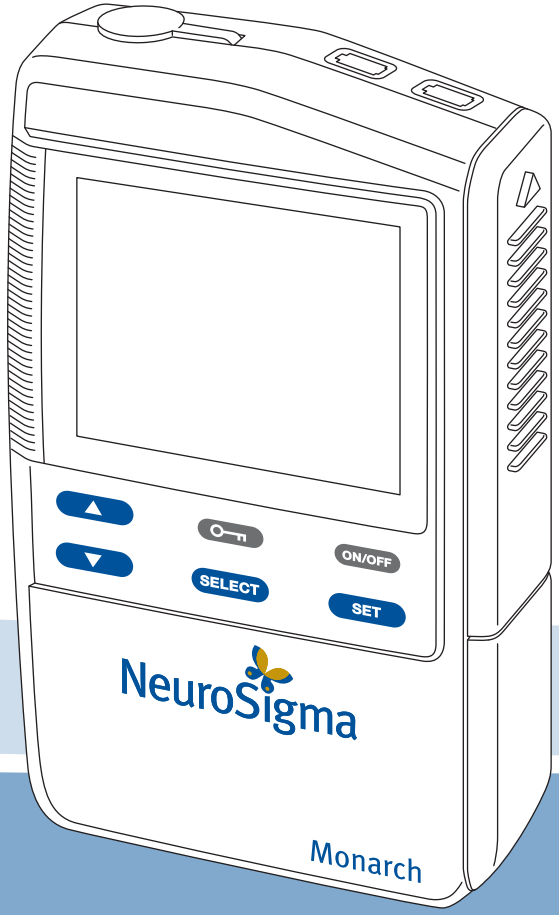
NeuroSigma

Monarch®

User Manual



Rx Only

CE 0086

Caution: Federal law restricts this device to sale by or on the order of a physician

CONTENTS

Please read this manual carefully before beginning treatment. It is an essential part of the *Monarch*® eTNS® System. This manual should be saved for future reference.

Caution: Federal law restricts this device to sale by or on the order of a physician.

I. Labeling Definitions and Symbol Descriptions

Caution: Pay special attention to the following details or consult accompanying documents

Type BF Applied Part

By order of a physician (not applicable in the EU)

Manufacturer

Conformité Européenne (European Conformity). This symbol means this device fully complies with MDD Directive 93/42/EEC

Temperature limitations

Use by date

I. Labeling Definitions and Symbol Descriptions (continued)

EC REP	Authorized representative in the European community
SN	Serial number
	Do not reuse
	Refer to instruction manual
	Operating instructions
REF	Product number
LOT	Lot number
	Unsafe within the magnetic resonance environment
	Recycle product separate from other disposables

II. Contraindications, Warnings and Precautions

READ ALL INSTRUCTIONS BEFORE USING

⚠ Contraindications

The device is contraindicated for use by patients with:

- implanted cardiac and/or neurostimulation systems
- implanted metallic or electronic device in their head

Do not use the *Monarch* eTNS System:

- in children under the age of 7 years
- in patients with body worn devices (e.g. insulin pumps and t-VNS)
- within 100cm of RFID readers or emitters that operate below 150kHz
- in the presence of the following sources of radio frequency (RF) energy:
  - MRI
  - Diathermy
  - Cell phones
  - CT
  - Microwave or shortwave
  - Metal detectors
  - RFID tags
  - Electronic article surveillance systems
  - TV transmission lines
  - High frequency (HF) equipment (e.g. surgical cauterizing tools and welding equipment)

Do not attach the electric patches:

- anywhere on the body other than the forehead
- on the neck
- on the chest
- over a defect in the skull (i.e. post brain surgery or head trauma) or over an open fontanel

II. Contraindications, Warnings and Precautions (continued)

⚠ Adverse Events

eTNS is generally well-tolerated. However, during the eTNS pivotal study, the following events occurred at a higher rate in the group treated with the eTNS system compared to subjects treated with the sham (placebo) device. Patients should consult their physician if any of the following events are observed:

- Bronchitis
- Headache
- Itching
- Lightheadedness
- Nausea
- Poor appetite
- Skin rash
- Stomach ache
- Tooth pain
- Vomiting
- Trouble sleeping
- Nightmares
- Drowsiness
- Fatigue
- Tingling
- Rapid heartbeat
- Constipation
- Frequent urination
- Increased appetite
- Clenching teeth

II. Contraindications, Warnings and Precautions (continued)

Warnings

Children 7 to 12 years receiving eTNS treatment should be closely supervised by an adult who has read the user manual and is familiar with the *Monarch* eTNS System.

The *Monarch* eTNS System should:

- only be used by the individual for whom it is intended.
- be used with the guidance of a licensed physician.
- be used with caution in patients with heart disease or serious medical disorders.
- be kept out of the reach of infants and children under the age of 7 years.
- be used only as directed and be applied to healthy, clean, intact skin.
- not be used with other electronic therapeutic devices.
- not be applied on the neck or chest.
- not be used in the presence of electric monitoring equipment (e.g. cardiac monitors).
- not be used in the bath or shower.
- not be used while operating machinery.

The *Monarch* electric patches should not:

- be used in patients with dermatitis or sensitive skin, as they are at higher risk of developing irritation.
- be used over broken, infected, or inflamed skin.
- be removed carelessly as this may damage the skin.

The *Monarch* lead wires should not be allowed to wrap around the neck.

The safety of the *Monarch* is unknown in the following conditions:

- trigeminal neuralgia or injury to the trigeminal nerve
- pregnancy
- concurrent use of hearing aids

The long-term effects of using the *Monarch* eTNS System are unknown. The effectiveness of the *Monarch* for long-term use in the indicated population (i.e. for more than 4 weeks) has not been systematically evaluated in controlled trials. Therefore, the physician who elects to use the *Monarch* for extended periods in patients with ADHD should periodically re-evaluate the long-term usefulness of the device for the individual patient.

III. Indications For Use

The *Monarch* external Trigeminal Nerve Stimulation (eTNS) System is indicated for treatment of pediatric Attention Deficit Hyperactivity Disorder (ADHD) as a monotherapy in patients ages 7 through 12 years old who are not currently taking prescription ADHD medications.

The device is to be used for patient treatment by prescription only and is intended to be used in the home under the supervision of a caregiver during periods of sleep.

IV. Trigeminal Nerve Stimulation Therapy

The main role of the trigeminal nerve is to convey sensation information from the face into the brain. External trigeminal nerve stimulation (eTNS) uses this natural pathway to send therapeutic signals into the brain. The trigeminal nerve connects directly from the face to the brainstem, and from there information is sent to other key brain regions thought to be involved in medical conditions such as ADHD (alternatively called hyperkinetic disorder or HKD). While the exact mechanism of action of eTNS is not yet known, neuroimaging studies have shown that eTNS increases activity in brain regions that are known to be important in regulating attention, emotion, and behavior. These findings are supplemented by basic science studies in animals, as well as clinical studies in humans. For more information on eTNS, please visit www.monarch-etns.com.

V. General Description

The *Monarch* eTNS System is designed to deliver electrical stimulation to branches of the trigeminal nerve, located just below the skin above the eyebrows, via a cutaneous electric patch.

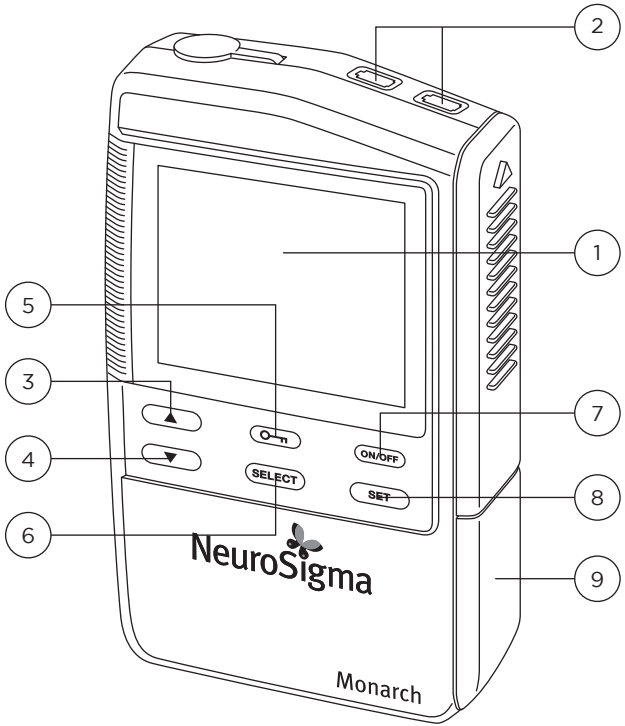
Main component

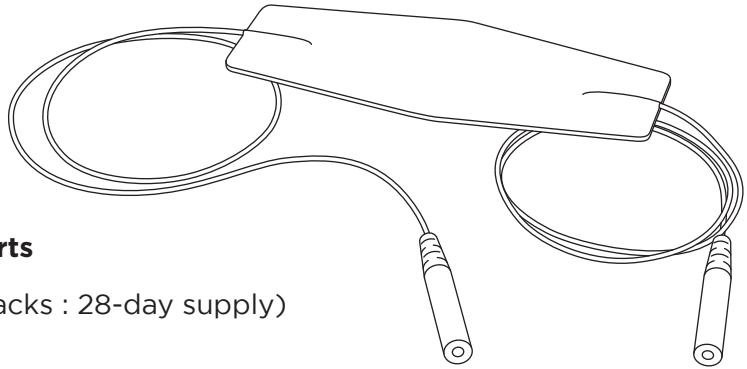
Monarch (external pulse generator)

1. LCD Screen
2. Output Ports (CH1, CH2)
3. Up Key
4. Down Key
5. Lock Key
6. SELECT Key

7 ON/OFF Key

8. SET Key
9. Battery Cover





Standard accessories and spare parts

Monarch electric patches (Four 7-packs : 28-day supply)
Lead wires (2)
NeuroSigma rechargeable 9-volt batteries (2)
NeuroSigma battery recharging station (1)
NeuroSigma battery recharging station AC adapter (1)
Belt clip (1)
Monarch User Manual (1)
Monarch carrying case (1)

⚠ Use only NeuroSigma approved accessories and spare parts. Use of unapproved accessories may cause personal injury, loss of therapeutic effect, equipment damage and will void manufacturer's warranty.

VI. *Monarch* Key Functions

SELECT key SELECT

Pressing the SELECT key selects output channels in the following sequence:

- CH-1 (Channel 1)
- CH-2 (Channel 2)
- CH-1 & CH-2 (both channels)

The selected channel blinks.

SET key SET

Pressing the SET key finalizes the selected item and stops the selected item from blinking.

Returns screen to selection mode if ERR is displayed.

Up and Down keys ▲ ▼

These keys are for setting or changing the current amplitude (intensity) in 0.2 mA increments. Keeping the key depressed will cause the current amplitude to increase or decrease with the key is depressed.

The current amplitude cannot be increased while the *Monarch* is not providing stimulation (Off Cycle).

▲KEY INVALID will be displayed at the top of the LCD screen during the Off Cycle.

Lock key

Pressing the Lock key locks all the keys except the Lock key itself. LOCKED will be displayed at the top of the LCD screen.

To unlock, press the Lock key for two seconds or longer.

ON/OFF key

This key turns the power on and off.

VII. Operating Procedures

Before Treatment

Set switch on side of battery charging station to “Li” (lithium).

Plug charging station into an electrical outlet (AC mains).

Insert battery into charging station.

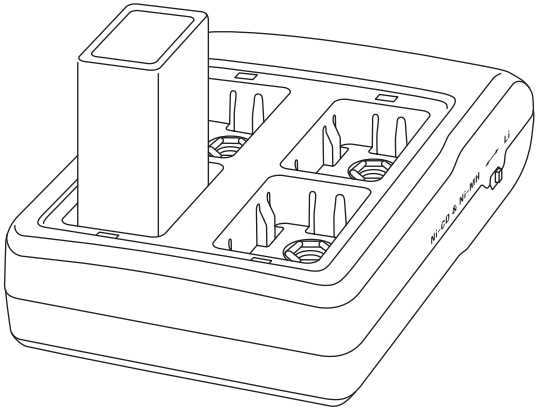
The LED light will glow red when the battery is charging.

Charging a battery can take up to one hour.

If the LED light flashes (red or green), then this battery cannot be charged and must be disposed according to local law.

The LED light on the charging station, above the battery will glow green when fully charged.

Remove battery from the charging station.



Insert a fully-charged battery as follows:

Slide the battery cover retainer upwards. (1)

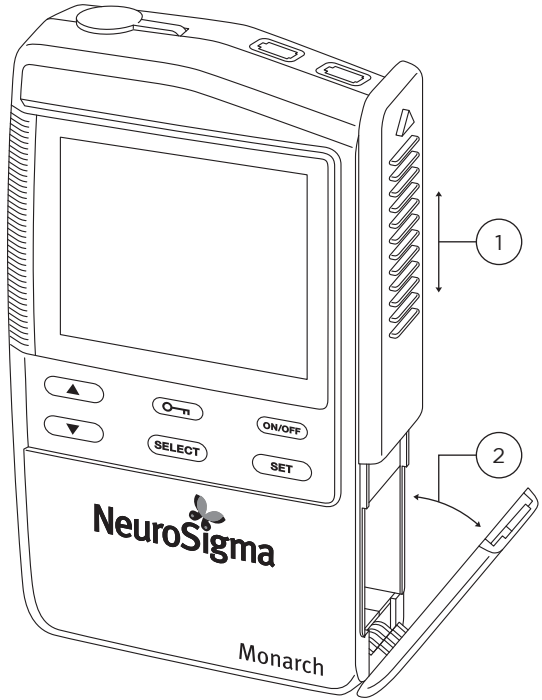
Pull the battery cover open. (2)

Place the battery into the battery case.

Be sure to align the positive and negative terminals on the battery with the markings inside the case. The case will not close if the terminals do not match.

Close the battery cover and return the retainer to its original closed position.

If the low battery symbol appears, replace with a fully-charged battery.



⚠ Use of a partially-charged battery may cause the *Monarch* to turn off before the treatment has completed.

If the *Monarch* will not be used for more than two days, remove the battery.

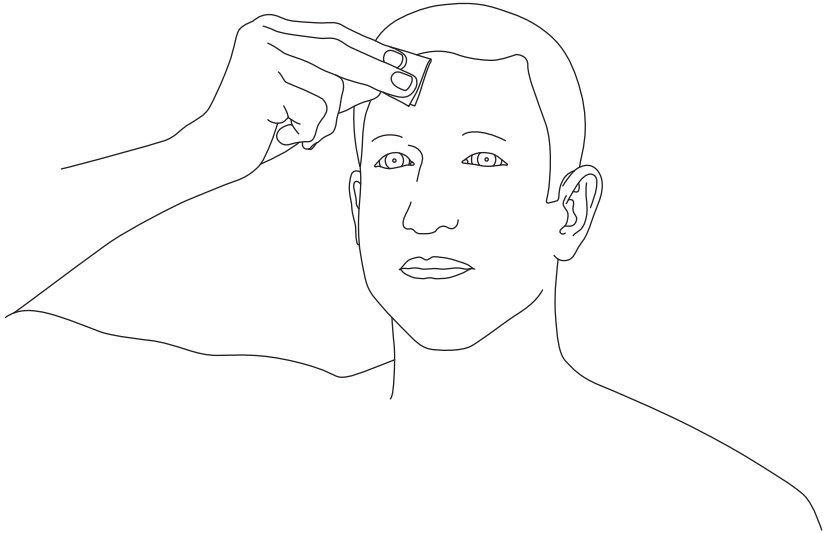
Use only NeuroSigma approved rechargeable batteries. Using unapproved batteries (rechargeable or non-rechargeable) may cause loss of therapeutic effect, fire or explosion.

Disposal of batteries should be done according to local law.

VII. Operating Procedures (continued)

Clean the skin of the forehead
with soap and water
or an alcohol-based cleaning pad.

Completely dry the skin.

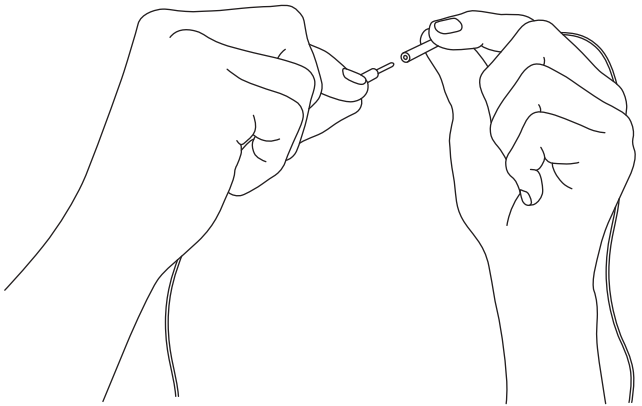


Remove electric patch
from the release liner backing.

Using a mirror, center the patch
on the forehead and apply
just above the eyebrows.

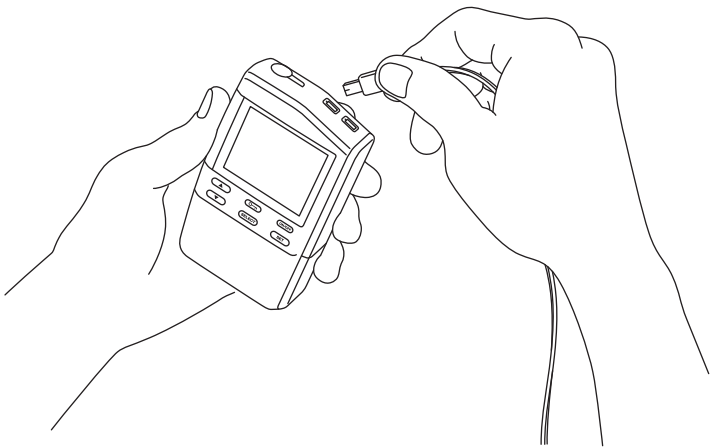
Be sure the patch is securely
and completely attached to the skin.

Connect electric patch wires to the lead wires. Place wires above and over the ears.



Insert lead wire plug into one of the two output ports (CH-1 or CH-2) of the *Monarch*.

Be sure the lead wire is securely connected in one of the output ports.



Treatment

Press the ON/OFF key

LCD screen will turn on. NeuroSigma will flash three times, followed by eTNS.

Press any of the four blue keys: Up, Down, SELECT or SET.

The screen will display Password.

Enter the password by pressing these keys in the following order: SELECT - ▲ - ▼ - SET.

CH-1, CH-2 and the Timer setting will appear on the screen.

CH-1 will be automatically selected (blinking). Current amplitude will be set at 0.0mA.

You may choose CH-2 by pressing the SELECT key. Be sure the lead wire is connected to the selected output port.

Press the UP key to increase current amplitude to maximum tolerable level. Stimulation should not be painful or uncomfortable.

Once the desired current amplitude is set, press the SET key then press the Lock key. The screen will display LOCKED at the top and the symbol will be displayed at the bottom left. All the controls other than the Lock key will be disabled. To unlock, press the Lock key for two seconds or longer.

You may attach the *Monarch* to your clothing using the belt clip provided.

When using the Monarch during sleep, the device can be worn, placed under a pillow or on a bedside table.

Course of Treatment

At least eight hours of continued use is recommended. Consult your physician for recommended duration of treatment.

Caregivers should look for skin irritation at the site where the electric patch is placed prior to and following the use of the device.

Clinical trials suggest that a clinical response to eTNS should be seen within 4 weeks.

Limited long-term data is available. Once a clinical response is achieved, continued therapy may be necessary. Consult your physician.

In case of skin irritation, stop use and consult your physician.
Do not apply electric patches to broken, inflamed or infected skin.

Do not attempt to clean or reuse electric patches. Dispose after a single use.

⚠ A sudden, electric stimulus, bothersome to some users, may be experienced under the following conditions:

- When a lead wire is broken.
- When the contact at the following locations is poor:

Between the patch and the skin.
At the connection between the patch wire and the lead wire.
At the connection between the lead wire and the *Monarch*.

In the instance of a sudden electric stimulus, replace the lead wire and electric patch and restart treatment at a low current amplitude. If the sudden stimulus continues, stop using the *Monarch* and contact your physician immediately.

The message ERR will appear at the top of the LCD screen when the *Monarch* detects an interruption in any of the connections within the *Monarch* eTNS System. This message will also appear if the user adjusts the current amplitude either without connecting the lead wires or adjusts the current amplitude on the incorrect output channel.

To clear the ERR message, make sure all the connections between the *Monarch* unit, the lead wires, and the patch are secure.

If the ERR message does not clear, try another lead wire and/or output channel until the message clears.

⚠ The message ⚠KEY INVALID periodically appears at the top of the LCD screen and means the *Monarch* is in an Off Cycle and that it is not currently providing electrical stimulation. This is normal and indicates the *Monarch* is functioning properly. During this Off Cycle the current amplitude cannot be increased, but it can be decreased.

If you wake up and the *Monarch* is powered off, first make sure all the connections are intact. Then, press the ON/OFF key. If the *Monarch* does not turn on, remove the battery and insert a fully-charged battery. Press the ON/OFF key again. If there are recurrent device turn-offs, contact your physician.

Be sure to always begin treatment with a fully-charged battery and to lock the *Monarch* after adjusting the settings.

After Treatment

When treatment is complete, unlock the *Monarch* by pressing the LOCK key for two seconds.

Turn the *Monarch* off by pressing ON/OFF key.

Unplug the lead wire from the *Monarch*.

Unplug the lead wire from the electric patch wire.

Gently remove the electric patch and dispose. Do not reuse.

Gently wash or clean skin of the forehead.

VIII. Maintenance and Cleaning

Cleaning Instructions

The *Monarch* can be cleaned with a cloth dampened with either water or a mild cleaning solution. Do not apply water or cleansers directly to any part of the *Monarch* eTNS System. Completely dry any component with a non-abrasive cloth before initiating treatment.

⚠ Do not clean the device while in use.

Do not make any alterations or repairs to the *Monarch* or to any of the components in the eTNS System, as this may result in personal injury, damage to equipment and voiding the manufacturer's warranty.

The *Monarch* may be damaged by dropping, shaking or rough handling, which may result in device malfunction, loss of treatment effect and personal injury.

Store the *Monarch* eTNS System in a dry environment avoiding excess humidity, temperature, sunlight and dust.

Do not store near chemicals or gases.

⚠ Cautions

The *Monarch* eTNS System generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause interference to other devices in the vicinity. However, there is no guarantee that interference will not occur in any particular installation. If this equipment does cause interference to other devices, try to correct the interference by one or more of the following measures:

- Reorient or relocate the receiving devices.
- Increase the separation between the equipment.
- Consult the manufacturer or field service technician for assistance.
- Electronic monitoring equipment (such as ECG monitors and ECG alarms) may not operate properly when eTNS stimulation is in use.

IX. Environmental Specifications

Guidance and Manufacturer's Declaration - Electromagnetic Emissions

Medical electronic devices are designed to ensure electromagnetic compatibility (EMC).

Portable and mobile RF communications devices may affect medical electronic devices.

Do not place the *Monarch* next to or on top of another device when using it. If it has to be placed next to or on top of another device, check that this instrument and the device function properly before use. If accessories other than those supplied as spare parts by NeuroSigma are used, the emission of the *Monarch* may increase and immunity may be reduced.

The *Monarch* eTNS System is intended for use in the electromagnetic environment specified in the following tables. The customer or the user of the *Monarch*® should assure that it is used in such an environment.

Emissions test	Compliance	Electromagnetic Environment— guidance
RF emissions CISPR 11	Group 1	The *Monarch* uses RF energy for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The *Monarch* is suitable for use in all establishments including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/flicker emissions IEC 61000-3-3	Complies	

Guidance and Manufacturer's Declaration – Electromagnetic Immunity

Part 1

Immunity Test	IEC 60601-1-2 test level	Compliance level	Electromagnetic environment - guidance
Electromagnetic discharge (ESD) IEC 61000-4-2	± 6 kV contact ± 8 kV air		Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Electrical fast transient/ burst IEC 61000-4-4	± 2 kV for power supply lines ± 1 kV per input/output lines		Not applicable. There is no connection to a.c. mains.
Surge IEC 61000-4-5	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth		Not applicable. There is no connection to a.c. mains.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	<5% *Ur* (>95% dip in *Ur*) for 0.5 cycle 40% *Ur* (60% dip in *Ur*) for 5 cycles 70% *Ur* (30% dip in *Ur*) for 25 cycles <5% *Ur* (>95% dip in *Ur*) for 5 seconds		Not applicable. There is no connection to a.c. mains.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-6	3 A/m		Power frequency fields should be at levels characteristic of a typical location in a typical commercial, hospital or domestic environment.

NOTE: *Ur* is the a.c. mains voltage prior to application of the test level.

Guidance and Manufacturer's Declaration – Electromagnetic Immunity

Part 2

Immunity Test	IEC 60601-1-2 test level	Compliance level	Electromagnetic environment - guidance
			Portable and mobile RF communications equipment should be used no closer to any part of the *Monarch*, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. ***Recommended separation distance:***
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz	3 Vrms	$d = 1.2\sqrt{P}$
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2.5 GHz	3 V/m	$d = 1.2\sqrt{P}$ 80 MHz to 800 MHz $d = 1.2\sqrt{P}$ 800 MHz to 2.5 GHz Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey,[a] should be less than the compliance level in each frequency range.[b] Interference may occur in the vicinity of equipment marked with the following symbol:

NOTE 1: At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios,amature radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the *Monarch* is used exceeds the applicable RF compliance level above, the *Monarch* should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the *Monarch*.

b Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3V/m.

Recommended Separation Distances Between Portable and Mobile RF Communications Equipment and The *Monarch* eTNS System

The *Monarch* is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the *Monarch* can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the *Monarch* as recommended below, according to the maximum output power of the communications equipment.

Rated maximum output power of transmitter (W)	Separation distance according to frequency of transmitter (m)		
	150 kHz to 80 MHz $d = 1.2\sqrt{P}$	***80 MHz to 800 MHz*** $d = 1.2\sqrt{P}$	***800 MHz to 2.5 GHz*** $d = 2.3\sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	12	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23

For transmitters rated at a maximum output power not listed above, the recommended separation distance (*d*) in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE 1: At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

NOTE 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects, and people.

X. Electrical Specifications

Supply voltage:	*Monarch* unit 9 V DC
Type of device:	Internally powered equipment/Type BF applied part
Dimensions:	69 mm (Width) x 115 mm (Length) x 27 mm (Depth)
Weight:	145 g (without battery)
Display:	LCD
Tested durability:	Service life (*Monarch* main unit): 5 years
	*Components (e.g., electric patches) are consumables
Error functions:	Battery error and open error only
Battery life:	Approximately 15 hours at standard clinically useful settings
	Li-Polymer, 9 V, 520 mAh, rechargeable battery
	Service life: 300 charges per battery (10 months each)
Accuracy of Measuring Functions:	All readings were taken between 0.2mA to 10.0mA Frequency: 120 Hz Pulse Width: 250µSec Load: 500Ω Error range: -48% at 0.2mA to +7% at 7.0mA

XI. Electrical Stimulation

Parameters	Specification
Intensity $I_{0\text{-}P}$(mA)	0 - 10 mA
Step (increment)	0.2 mA
Time	1, 4, 6, 8, 10, 12, 16 hour and continuous
Lock Mode	Locks all buttons except itself (Lock button). Press for two seconds to unlock.
Input code (password)	Restricts use for intended patient

XII. Environmental Conditions

Operating environment: 10°C to 40°C, 30% to 75%, 700 to 1060 hPa

Storage environment: -10°C to 60°C, 30% to 95% (condensation allowed), 700 to 1060 hPa

Transport environment: -10°C to 60°C, 30% to 95% (condensation allowed), 700 to 1060 hPa

XIII. Clinical Data

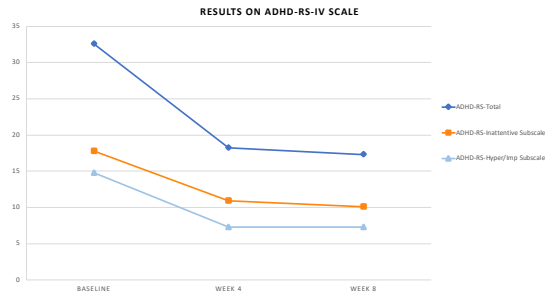
Pilot Study

The pilot study was an 8-week, single arm, open label trial designed to assess the safety, tolerability, and initial efficacy of the *Monarch* eTNS. The subjects were aged 7 - 14 years old and were diagnosed with ADHD based on DSM-IV criteria.[1] Of the 24 subjects who initiated the study, 22 subjects completed the week 4 efficacy assessment and 21 completed the week 8 efficacy assessment, indicating a high level of tolerability for therapy with eTNS.

There were no serious adverse events associated with use of the device. Of the spontaneously reported adverse events, only headache (n = 2) and eye twitch (n = 1) were considered potentially device-related; all of these resolved spontaneously and did not inhibit trial participation. eTNS achieved a statistically significant improvement on the trial's primary endpoint, the ADHD-IV Rating Scale ("ADHD-RS"),[2] at weeks 4 and 8. Mean scores improved from 32.6 points at baseline to 18.2 points at Week 4 and 17.3 points at Week 8 ($p < 0.0001$).

Although not tested for statistical significance, assessment of subjects using the Clinical Global Impression – Improvement (CGI-I)[3] scale also demonstrated that a large majority of subjects improved in their overall clinical conduction. Specifically, at Week 4 and 8, 64% and 71% of subjects, respectively, were assessed as being "improved" or "very improved". In addition, according to daily treatment diaries from subjects who completed the trial, nightly treatment compliance was 100%.

Results on ADHD-IV RS Scale



[1] DSM-IV – Fourth edition of the Diagnostic and Statistical Manual of Mental Disorders. The DSM-IV is the primary assessment tool in the US for diagnosing ADHD.

[2] Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS) – a parent rating scale that assesses the frequency of each ADHD symptoms identified in the DSM-IV criteria for the disease.

[3] Clinical Global Impression – Improvement (CGI-I): CGI-I is a physician rated assessment taken by interviewing the patients. The physician compares the patient's overall clinical condition to the week just prior to starting treatment and rates the comparison on a scale of 1 (very much improved) to 7 (very much worse). A score of 1-3 is associated with improvement, a score of 4 is no change, and a score of 5-7 is associated with deterioration.

XIII. Clinical Data (continued)

Pivotal Study

The pivotal study was a prospective, double-blind, randomized controlled trial of the *Monarch* eTNS as monotherapy for pediatric ADHD, with 4 weeks of treatment. The study enrolled 62 children (32 active; 30 sham) who had been diagnosed with moderated to severe ADHD. Fifty-nine (59) subjects completed the four-week double-blind treatment period (31 active and 28 sham).

The average subject age was 10.4 years (range 8-13 years old). Sixty-five percent (65%) of subjects were male and thirty-five percent (35%) were female. The study population include White (65%), Black (6%), Asian (16%), and Mixed/Other (13%) races. The study population was 16% Hispanic. Sixty-three percent (63%) of subjects had the combined subtype of ADHD, thirty-four percent (34%) had the inattentive subtype, and three percent (3%) had the hyperactive/impulsive subtype.

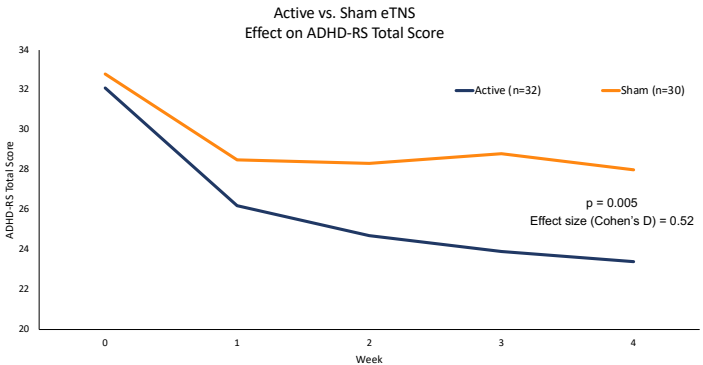
The subjects received nightly treatments with either the active or sham device. The primary endpoint, as in the pilot study, was improvement on the clinician-administered ADHD-RS (weekly assessments). The CGI-I assessment was also administered.

XIII. Clinical Data (continued)

Pivotal Study (continued)

The trial met its primary efficacy endpoint. At the end of Week 4, the average ADHD-RS score in the active group decreased from 34.1 points at baseline to 23.4 points, versus a decrease from 33.7 to 27.5 points in the sham group. Using the GLMM methods for statistical analysis, it was found that the mean ADHD-RS scores showed differential group effects in favor of active eTNS as demonstrated by a significant group by time interaction (p = 0.005).

Mean ADHD-RS Total Score by Time Point by Group

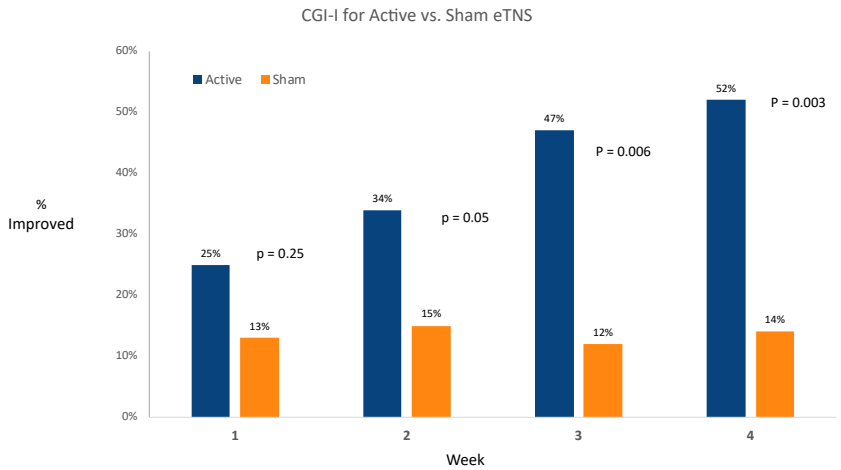


The CGI-I scale results demonstrated a statistically significantly greater improvement in the active arm than the sham arm, when subjects were either classified as "improved" based on receiving a CGI-I score of 1 or 2 (i.e. "very improved" or "improved" on the assessment scale) or "not improved" based on a score ≥ 3. At Week 4, 52% of active subjects were classified as "improved" compared to only 14% of subjects in the sham arm (p = 0.003). Note, in the active group the percentage of subjects classified as "improved" rose each consecutive week, compared to the sham group which remained flat.

XIII. Clinical Data (continued)

eTNS was well-tolerated in all 62 subjects and there were no serious adverse events (SAEs) associated with use of the device. Commonly reported side effects among all pivotal study subjects included trouble sleeping, hyperactiveness, drowsiness, and stuffy nose, but there was no statistically significant difference between the active and sham groups for these events. Events that were more common in the active group than the sham group included: nightmares (6% versus 0%), headache (13% verus 0%), frequent urination (6% versus 0%), increased appetite (19% versus 7%), skin rash (6% versus 0%), and teeth clenching (13% versus 7%). The between group difference for these events was not statistically significant, except in the case of headache (p = 0.05). Weight gain was only slightly greater in the active group compared to the sham group (0.6 kg) and was not clinically meaningful given the age group. As noted above, no participant left the study due to side effects or adverse events in either the pilot or pivotal study. However, all reported side effects and adverse events were of low to moderate severity and most were transient.

Percent of Group Reporting Improvement on CGI-I Scale



XIII. Warranty

NeuroSigma, Inc. warrants the *Monarch* eTNS System against any defect in materials and workmanship for a period of two (2) years from the purchase date. Please retain all invoices and sales receipts, since these are proof of the purchase date.

The warranty does not cover accessories and spare parts, including electric patches, lead wires, batteries and battery charging station. The warranty does not cover damage caused by rough handling, such as drops, shocks and exposure to water and other damaging environments. The warranty does not apply to devices whose cases and/or screens are crushed, cracked, broken, or buckled. During the warranty period, at the sole discretion of NeuroSigma, the *Monarch* device will either be repaired free of charge by an approved service provider or replaced.

To obtain warranty service, go to our website, www.monarch-etns.com, and complete the Return Material Authorization (RMA) form and either mail or email it to our office, using the contact information provided on the website. You can also call our Customer Service Department at the following telephone number: +1.310.479.3100.

NOTE: All warranty repairs and service must be performed by NeuroSigma.

NOTE: A complete listing of all warranty features and exclusions is included as part of your purchase invoice. Please refer to it for further details or go to our website, www.monarch-etns.com, and download a full copy of the *Monarch* eTNS System warranty.

For more information about eTNS therapy and the side effects reported to date, please contact NeuroSigma.

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