DE NOVO CLASSIFICATION REQUEST FOR
SYMPHONY DEVICE

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Vibratory counter-stimulation device.** A vibratory counter-stimulation device is a prescription device that provides electrically powered mechanical vibration to improve the quality of sleep in patients with primary Restless Legs Syndrome.

NEW REGULATION NUMBER: 882.5895

CLASSIFICATION: CLASS II

PRODUCT CODE: OVP

BACKGROUND

DEVICE NAME: *SYMPHONY*™ DEVICE

SUBMISSION NUMBER: DEN110011

DATE OF DE NOVO: JULY 13, 2011

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REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS II

INDICATIONS FOR USE

The purpose of the *Symphony* Device is to improve the quality of sleep in patients with primary Restless Legs Syndrome (RLS) through the use of vibratory counter-stimulation.

LIMITATIONS

For prescription use only.

Limitations on device use are also achieved through the following statements included in the Instructions for Use Manual:

Contraindication:

- This device should not be used on patients who have been diagnosed with deep venous thrombosis (DVT) in either leg during the last 6 months because of the known potential to dislodge or break up the clot and cause a pulmonary embolism.

Warnings:
The *Symphony* Device is only intended for use on patients with primary Restless Legs Syndrome (RLS). It is not intended to be used by people who:

- have leg skin disorders such as eczema, psoriasis, cellulitis, non-healing wounds; or
- have secondary RLS.

Due to the potential for the device to cause worsening of symptoms in some patients, the patient labeling should include a warning to discontinue device use and contact a doctor if symptoms worsen.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The *Symphony* Device is a non-sterile, reusable, cloth-covered foam pad that contains six embedded electric motors that swing eccentric weights to produce vibration throughout the pad. The device is designed to be placed under the user's legs while sleeping. When the device is activated, an electronic controller runs a 35 minute preset vibration cycle. The controller allows the patient to control the intensity level of the vibration for the first 30 minutes of the cycle. In the last five minutes, the controller slowly ramps down the vibration intensity of the device and then automatically shuts the device off at the end of the timed cycle. One repeat cycle can be initiated by the patient.

The controller contains the on/off function and has variable mechanical counter-stimulation intensity settings (1 to 9). The motor amplitude and frequency (vibration) can be set to different levels of intensity by means of a knob. The polyurethane foam pad is covered by an inner lycra cover and an outer cover. The outer cover on the *Symphony*™ Device is made of cotton. The device will be offered in three sizes: Small, Medium, and Large.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The *Symphony* is intended to only contact intact skin for a limited duration (< 24 hours). The patient-contacting, outer cover of the device is made of cotton. In lieu of biocompatibility testing, the sponsor provided a justification that the identical material has a demonstrated long history of safe use in legally marketed devices with the same type and duration of contact.

SHELF LIFE/STERILITY

The *Symphony* is a non-sterile, reusable device. It is intended only for external use and the user manual includes appropriate cleaning instructions for the removable outer cover.

The device does not have a stated shelf life, which, based upon the nature of the device components, is acceptable.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The *Symphony* device was tested for and found to be in compliance with the following standards for electromagnetic compatibility and electrical safety:

Standard	Title
IEC 60601-1	Medical electrical equipment – Part 1: General requirements for safety.
EN 55011	Limits and methods of measurement of radio disturbance characteristics of industrial scientific & medical (ISM) radio-frequency equipment
EN 61000-4-2	Electromagnetic compatibility (EMC) – Part 4-2: Testing and measurement techniques – Electrostatic discharge immunity test
EN 61000-4-3	Electromagnetic compatibility (EMC) – Part 4-3: Testing and measurement techniques – Radiated, radio-frequency, electromagnetic field immunity test
EN 61000-4-4	Electromagnetic compatibility (EMC) – Part 4-4: Testing and measurement techniques – Electrical fast transient/ burst immunity test
EN 61000-4-5	Electromagnetic compatibility (EMC) – Part 4-5: Testing and measurement techniques – Surge immunity test
EN 61000-4-6	Electromagnetic compatibility (EMC) – Part 4-6: Testing and measurement techniques – Immunity to conducted disturbances, induced by radio frequency fields

SOFTWARE

Software for the device consisted of firmware that controls the vibration cycle of the device. The software was reviewed and the provided documentation was found adequate and consistent with a 'MINOR' level of concern, as discussed in the FDA document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005.

PERFORMANCE TESTING – BENCH

Device outputs – Testing was conducted to characterize the device outputs at eachintensity setting on the controller. The mean, minimum, and maximum values of acceleration, velocity, displacement (amplitude), and frequency (rpm and Hz) were within specifications for each setting.

Device durability and safety – The following testing was conducted to characterize the *Symphony* device's ability to perform safely when subjected to different use scenarios: life cycle testing, decibel level, pad surface temperature, motor housing deformation, drop test, bend test, strain relief and electrical cable tensile strength, and shaft tensile strength.

SUMMARY OF CLINICAL INFORMATION

Two clinical trials were conducted to assess the safety and effectiveness of counter-stimulation with the *Symphony* Device in the treatment of patients with primary RLS. The primary difference between the two studies was the design of the sham device. The first study (SMI-001) used a sound-emitting (auditory) sham in the control group, while the second study (SMI-002) used a light-emitting sham control. Both studies had the same primary and secondary endpoints.

1. SMI-001

Design: This was a prospective, 1:1 randomized, multicenter (5 sites) trial which assessed the safety and effectiveness of the *Symphony* Device in the reduction of symptoms associated with RLS by comparison to an auditory sham control device. Subjects were adults with moderate to severe primary RLS involving only the legs, with a minimum baseline score of 15 points on the International Restless Legs Scale (IRLS) scale and symptoms occurring at least 15 nights per month. Patients with secondary RLS, other sleep disorders, disorders involving the legs (e.g., cellulitis, deep vein thrombosis) or taking unapproved medications to treat their RLS were excluded. If subjects were on an approved RLS medication, they were required to be on stable doses during the trial. Patients used the device for at least one 35 minute cycle each night. The primary endpoint was the mean change from baseline in the IRLS total score to week 1, 2, 3 and 4. The safety endpoint was a descriptive analysis of adverse events from both groups. Secondary endpoints included the mean change from baseline to 4 weeks in the Medical Outcomes Study (MOS) Sleep Scale scores and the Johns Hopkins Restless Legs Syndrome Quality of Life questionnaire (RLSQOL). The MOS inventory is a patient-reported questionnaire that evaluates sleep disturbance. The MOS sleep problem index I (MOS-I) contains 6 of the 12 inventory questions, while the MOS sleep problem index II (MOS-II) contains an additional 3 questions (9 of the 12). The scale measures sleep difficulty based on recall about sleep quality during the four weeks prior to taking the test.

Results: A total of 77 subjects were enrolled in the study at a 1:1 ratio (39 used *Symphony*, 38 used the sham device). Although there were no statistically significant differences between active and sham groups for the primary endpoint (IRLS score), there were statistically significant improvements in the mean MOS-I scores (-16.76 for *Symphony* vs -5.09 for sham, p=0.0117) and MOS-II scores (-15.83 for *Symphony* vs -5.34 for sham, p=0.0230).

Adverse Events: There were 7 AEs in the *Symphony* group (17.9%) and 1 in the sham group (2.6%) that were at least possibly device-related. There were an additional 2 AEs in the Symphony group and 3 AEs in the sham group that were not device-related. All device-related AEs resolved after use of the device was stopped, without medical intervention or clinical sequelae. One AE (cramping sensation in both legs) was graded as moderate and all 7 remaining AEs were graded as mild. The most common AE was worsening of RLS symptoms, which occurred in 4 subjects with the *Symphony* device (10.3%) and 1 subject with the sham device (2.6%). Worsening of RLS symptoms resolved within 3 weeks of discontinuation of device use without additional intervention. Other device-related AEs

reported in the *Symphony* group included non-RLS leg cramps (2 AEs, 5.1%) and leg soreness (1 AE, 2.6%).

2. SMI-002

Design: This was a prospective, 2:1 randomized, multicenter (4 sites) trial which assessed the safety and effectiveness of the *Symphony* Device in the reduction of symptoms associated with RLS by comparison to a light-emitting sham control device. The inclusion/exclusion criteria, study design, and endpoints were very similar to SMI-001, with only minor differences.

Results: A total of 81 subjects were enrolled in the study at a 2:1 ratio (52 used *Symphony*, 29 used the sham device). Although there were no statistically significant differences between active and sham groups in any of the primary or secondary endpoints, there were mean improvements in the MOS-I scores (-10.13 for *Symphony* vs -5.48 for sham, p=0.2358) and MOS-II scores (-11.41 for *Symphony* vs -7.36 for sham, p=0.3040) that did not achieve statistical significance.

Adverse Events (AEs): There were 5 AEs in the *Symphony* group (9.6%) and 2 in the sham group (6.9%) that were at least possibly device-related. There were an additional 2 AEs that were not device-related, both in the *Symphony* group. All device-related AEs in the *Symphony* group were categorized as worsening of RLS symptoms and resolved within 3 weeks of discontinuation of device use without additional intervention. One of these AEs was graded as moderate and the remaining 4 were graded as mild. In the sham group, 1 AE was categorized as worsening of RLS symptoms (mild), which resolved after stopping use of the sham device. The other AE was pain below the knee (moderate), which resolved with use of a heating pad.

LABELING

The *Symphony* User Manual is consistent with the clinical data and covers all the hazards and other clinically relevant information that may impact use of the device. The labeling is sufficient and satisfies the requirements of 21 CFR § 801.109 Prescription devices. Because the clinical data indicate that approximately 10% of patients using the *Symphony* device experience worsening of RLS symptoms, the patient labeling includes instructions to discontinue device use and contact a doctor if symptoms worsen.

RISKS TO HEALTH

The table below identifies the risks to health that are associated with use of vibratory counter-stimulation devices and the measures necessary to mitigate these risks.

Identified Risk	Mitigation Method
Pain, discomfort, worsening of RLS symptoms	Non-clinical Testing Software Testing Labeling
Electrical shock	Electrical Safety Testing Labeling
Burns	Electrical and Thermal Safety Testing Labeling
Adverse skin reactions	Biocompatibility Assessment Labeling
Interference with other medical devices	Electromagnetic Compatibility Testing Labeling

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the Vibratory Counter-Stimulation device is subject to the following special controls:

1. Appropriate analysis/testing must demonstrate electromagnetic compatibility (EMC), electrical safety, and thermal safety.
2. If the device contains software or firmware, appropriate verification, validation, and hazard analysis must be performed.
3. The elements of the device that contact the patient must be assessed to be biocompatible.
4. Non-clinical testing data (including vibration frequency, amplitude and acceleration) must demonstrate that the device performs as intended under anticipated conditions of use.
5. Labeling must include:
    a. Specific information pertinent to use of the device by the intended patient population and the treatment regimen.
    b. Warning to only use the device on normal, intact, clean, healthy skin.
    c. Warning to not use the device if the user has leg skin disorders, such as eczema, psoriasis, cellulitis, non-healing wounds.
    d. Warning to discontinue use if restless leg syndrome symptoms worsen.
    e. Instructions for end users to contact the device manufacturer and MedWatch in case they experience any adverse events when using this device.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

BENEFIT/RISK DETERMINATION

The risks of the device are based on data collected in the clinical studies described above. No serious device-related adverse events were reported in the clinical performance data. The majority of adverse events were minor and all resolved on their own within 3 weeks after discontinuation of device use. Based on this information, along with a demonstrated history of safe use of devices with similar technology (*i.e.*, therapeutic massagers), the risk associated with this device is considered low.

The probable benefits of the device are also based on data collected in two clinical studies as described above. Although the IRLS scores do not support that the device is effective for improvement of RLS symptoms in general, the data do indicate an improvement in the specific area of sleep quality. The SMI-001 clinical study demonstrated a statistically significant improvement in the 4-week mean MOS-I and MOS-II sleep scores compared to the control. Although the results of the SMI-002 study did not reach statistical significance, the mean reduction in MOS-I and MOS-II scores was greater than with the sham device. Overall, this indicates that there is clinical benefit for patients with primary RLS.

Additional factors to be considered in determining probable risks and benefits for the Symphony device include: (1) there are no legally marketed devices available for patients with RLS. There are approved drug treatments, but these have known adverse events that are more common and more severe than those seen in the *Symphony* trials. (2) Although RLS is a chronic disease, long-term safety and effectiveness data are not available. The clinical data is limited to 4 weeks in duration.

Given the available information above, the data support that for improving the quality of sleep in patients with primary Restless Legs Syndrome (RLS), the probable benefits outweigh the probable risks for the *Symphony*™ device. The device risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The *de novo* for the *Symphony* device is granted and the device is classified under the following:

Product Code: OVP
Device Type: Vibratory counter-stimulation device
Class: Class II
Regulation: 21 CFR 882.5895