DE NOVO CLASSIFICATION REQUEST FOR OSTEOBOOST BELT

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Wearable vibration device for orthopedic use. A wearable vibration device for orthopedic use is a wearable device that uses mechanical vibrations, targeted to specific regions of the skeleton, to reduce loss of bone strength or bone mineral density.

NEW REGULATION NUMBER: 21 CFR 888.5895

CLASSIFICATION: Class II

PRODUCT CODE: QZO

BACKGROUND

DEVICE NAME: Osteoboost Belt

SUBMISSION NUMBER: DEN230015

DATE DE NOVO RECEIVED: February 17, 2023

SPONSOR INFORMATION:

Bone Health Technologies, Inc.
370 Convention Way
Redwood City, California 94107

INDICATIONS FOR USE

The Osteoboost Belt is indicated as follows:

The Osteoboost Belt is indicated to reduce the decline in bone strength and volumetric bone density, as assessed via CT (computed tomography) scans that were analyzed using the O.N. Diagnostics_VirtuOst estimate of vertebral bone strength and density in postmenopausal women with osteopenia of the lumbar vertebrae or total hip as diagnosed via dual x-ray absorptiometry with a bone mineral density T-score between -1.0 and -2.49.

- The clinical effects have only been observed for the duration of the clinical study performed to support the indications for use (1 year).
- Fracture risk was not evaluated in the clinical study to support the indications for use, so it is not known how the treatment effects correlate with fracture risk.

- The clinical effects have been demonstrated only for those who used the device as indicated.

LIMITATIONS PER EXCERPTED LABELING FOR THE OSTEOBOOST BELT

- **WARNINGS**
  - This device is not indicated for patients with osteoporosis.
  - The device has been evaluated in a clinical study with a high majority of Caucasian women without high-risk factors for developing bone fragility, such as heavy smoking, type I diabetes, renal disease, or a history of fractures. The safety and effectiveness of the device has not been evaluated in a significant number of non-Caucasian women, in subjects with high-risk factors for developing bone fragility, or in subjects with a BMI > 35.
  - Let your doctor know before use of the Osteoboost if you have any of the following conditions: 1) are allergic to neoprene, 2) are being treated for a herniated disc, 3) have had a spinal fusion procedure, 4) have a joint replacement implant in the ankle, knee, or hip, or 5) have an active implant (e.g. implanted neurostimulator) in the areas of the lumbar or thoracic spine, pelvis, or buttocks.
  - Do not apply Osteoboost directly to the skin. Wear a thin layer of clothing between the device and the skin.
- **PRECAUTIONS**
  - Only charge the Osteoboost with the supplied charger.

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

LIMITATIONS OF THE CLINICAL STUDY DATA

- The clinical effects have only been observed for the duration of the clinical study performed to support the indications for use (1 year).
- Fracture risk was not evaluated in the clinical study to support the indications for use, so it is not known how the treatment effects correlate with fracture risk.
- The clinical effects have been demonstrated only for those who used the device as indicated.
- In the clinical study of the device, a very high majority of Caucasian patients were evaluated (under-represented non-Caucasian population). Therefore, the effect of using the device in non-Caucasian population is not clearly demonstrated.
- The safety and effectiveness of the device has not been evaluated in patient populations with high-risk factors for developing bone fragility or fractures, such as heavy smoking,

DEVICE DESCRIPTION

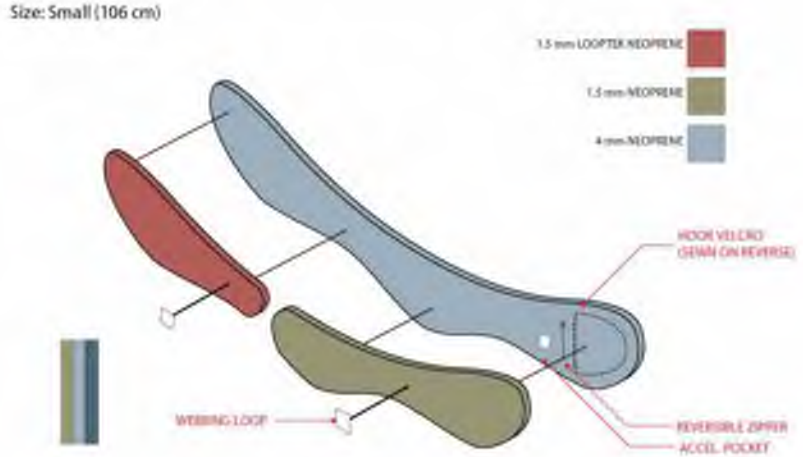
For a complete description of the device system components and subsystems, please refer to the accompanying labeling for additional details.

The Osteoboost is a wearable belt with an incorporated motor that is designed to transmit low-amplitude, high-frequency (20-40 Hz) vibration to the spine and hips. Osteoboost consists of a vibration pack mounted to a belt made of nylon-covered neoprene. The device is intended to be worn on top of a thin layer of clothing and positioned such that the vibration pack sits tightly over the sacrum. The device includes a pressure sensor under the foam pad to ensure that the device has been fastened with adequate pressure to transmit the vibration correctly. In addition, the belt incorporates an accelerometer positioned at the iliac crest which measures the actual transmission of vibration to the skeleton.

Figure 1. Front view of the Osteoboost: (1) Nylon-covered neoprene belt, (2) vibration pack (housed on the back of the neoprene belt), (3) inner Velcro, (4) nylon straps, (5) clasp, (6) power button, (7) battery status light, (8) attention light, (9) hip accelerometer (located in the neoprene belt).

Belt

The Belt is comprised of several layers of neoprene, to which were added Velcro fasteners, nylon webbing loops, a zipper, and component pockets. Each layer of neoprene has a thin nylon fabric laminated on either side. The middle structural layer, which is 3 mm thick, supports most of the weight of the vibration pack and provides some rigidity. The outer layers of neoprene are 1 mm thick.



Vibration Pack

The vibration pack uses a battery-powered rotating-mass motor controlled by pulse-width modulation (PWM) with duty cycle that can be tuned to change the rotation frequency and amplitude (over the motor frequency range of 20-40 Hz). The motor is attached to and oriented within the pack so to transmit vibration to the patient primarily in the sagittal plane (x- and z-axes, where the z-axis is parallel to the patient's height axis/long body axis).

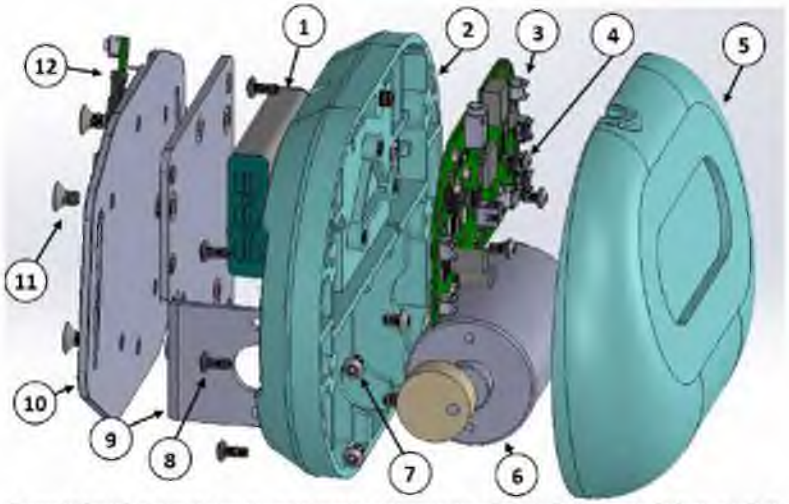


Figure 8. Exploded view of vibration pack showing (clockwise from top): (1) Battery pack (2) Bottom half of housing (3) PCBA (4) PCBA screws x 3 (5) Top half of housing (6) Motor (7) Motor mounting screws (2 in total) (8) Housing screws (7 in total) (9) Motor mount plate (10) Back plate (11) Belt attachment screws (6 in total) (12) Force sensor.

Software

The only software for the device is the firmware on the Osteoboost. There are no mobile medical apps or separate software associated with the subject device. The software controls the power level at which the motor operates along with data from all peripherals including the belt-fit force sensor, accelerometers, motor driver, and the battery's fuel gauge and records this information to an onboard flash chip. It also monitors device functionality, such as battery temperature and motor current.

Accelerometers

The Osteoboost has two accelerometers. The main accelerometer, embedded within the neoprene belt, is used to quantify transmission of acceleration from the pack to the patient. A secondary accelerometer is located on the PCBA (Printed Circuit Board Assembly) proximal to the motor, where it is used to monitor motor activity directly. The accelerometers utilize MEMS (Micro-Electro-Mechanical Systems) technology. There are several sensors in Osteoboost which have a maximum range of ±16 g (although this range is set to ±4 g in practice to increase sensitivity) and is capable of high-resolution data rates up to 1.6 kHz.

Battery

The device is powered by a rechargeable lithium ion (Li-ion) 2000 mAh battery pack (RRC1120, RRC Power Solutions, Yorba Linda, California). The battery can last at least 3 treatment sessions before needing to be recharged. The battery is recharged using a supplied 5-V AC-DC power supply (wall wart) which plugs into a standard 120/240V outlet. The battery pack

complies with all applicable safety standards including: UL2054, IEC62133, UN38.3, RoHS, REACH, and TIS 2217-2548.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The device is intended to be worn on top of a thin layer of clothing and the device does not contact the patient directly or indirectly. Based upon a biocompatibility risk assessment following the FDA guidance document "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process'", biocompatibility testing was not needed for this device.

SHELF LIFE/STERILITY

The subject device is a non-critical, non-sterile, single patient use device, that is for use in the home environment and is not expected to be used in a healthcare environment. Reprocessing instructions are included in the labeling. Any additional cleaning beyond what is currently stated in the instruction for use is not needed. There is no shelf life for this device.

Package performance testing was tested to ISTA-6-FEDEX-A, a specific test protocol created to perform the testing applicable to ISTA 3A (Recognition Number 5-126) but specifically formulated to cover the environmental conditions experience during FedEx air and ground shipping of packages weighing up to 150 lbs. One of each size of device (small, medium, and large) was packaged, shipped via FedEx, and tested according to ISTA-6-FEDEX-A.

ELECTROMAGNETIC CAPABILITY & ELECTROMAGNETIC SAFETY

Electromagnetic compatibility and electrical safety testing were performed in accordance with the following standards:

- IEC 60601-1:2012 Medical electrical equipment Part 1: General requirements for basic safety and essential performance;
- 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;
- IEC 60601-1-11:2015 Medical electrical equipment — Part 1-11: General requirements for basic safety and essential performance — Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment.

The objectives of the series of tests to support electromagnetic compatibility and electrical safety, included the following:

- The device should operate normally following exposure to a simulated electrosurgical environment and shall not exhibit unintentional radiated emissions above recommended limits.
- The device should meet performance requirements related to radiated power, receiver sensitivity, frequency range, channel bandwidth and out-of-band power.
- The testing should verify that the device does not exhibit unintentional radiated emissions above recommended limits and is immune to electrosurgical equipment.
- The testing should assess the electrical safety and usability of the subject device components in the appropriate use setting.
- The testing should assess the safety, compatibility, radio frequency, and magnetic immunity.

The test results supported electromagnetic compatibility and electrical safety of the device use in its worst-case running mode.

SOFTWARE

Software Description

The Osteoboost device includes embedded firmware to control the operation of the device by the user. This medical device software is only active when the device has been turned on and deactivates when the device has been turned off. While the device is operating, the main routines of the software can be broken down into three categories:

- **Motor Control**
  The motor power level is controlled by sending a Pulse-Width Modulated (PWM) signal from the processor to the motor driver.
- **Data collection**
  During the calibration phase, the motor PWM is set to the default value, and acceleration amplitudes are recorded from the accelerometers located on the hip and on the back (near the motor).
- **Device monitoring**
  The software continuously monitors the belt-fit force sensor to ensure adequate pressure is being applied to the patient. The software also continuously monitors the battery temperature and fuel gauge, the motor driver current limits and software watchdogs.

Verification testing

Software verification testing activities were performed for the software components to verify that the system functions as designed. Testing of the software components occurred at the unit, integration, and system level, as appropriate. Following completion of the verification procedures, all features pertaining to pressure sensing and modulating

the vibration speed of the accelerometers to deliver the therapeutic treatment passed the testing acceptance criteria.

Revision Level History
The current version of firmware component is as follows:

Embedded firmware-Version 3.0
C-programming

PERFORMANCE TESTING - BENCH

- **Battery Safety and characterization testing**
  The battery testing on the safety of the rearrangeable Lithium-Ion battery cell used in the Osteoboost Belt was conducted according to IEC 62133-2:2017, Secondary cells and batteries containing alkaline or other non-acid electrolytes - Safety requirements for portable sealed secondary cells, and for batteries made from them, for use in portable applications - Part 2: Lithium systems and was found to be in compliance with the standard.

- **Alarms system testing**
  The alarm systems in the Osteoboost Belt followed IEC 60601-1-8 ("General requirements for basic safety and essential performance - Collateral Standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems") and was found to be compliant with the standard. Risk controls were implemented based on the Use Failure Mode Effects Analysis.

- **Bench verification testing for Constant Acceleration Throughout the Use-Life of the Device**
  A verification test was performed to evaluate whether the device is capable of generating a constant acceleration throughout the use-life of the device, including both during each individual charge/discharge cycle of the battery, and across the use-life of the battery. To confirm the motor frequency does not vary over the lifetime of the device, the motor was run at a set input with a fully charged battery, the motor frequency was measured using a tachometer, and the motor continued to run over the range of voltages provided by the battery until it was fully depleted. The motor frequency variability was calculated over the life of the battery, and a percentage deviation from worst-case condition was provided. The acceptance criteria of the motor frequency remaining consistent throughout the battery voltage cycle and maintain within a range of approximately ±1% was met.

- **Testing to evaluate the Range of Vibration Transmission to Targeted Anatomic Locations**
  A verification test was performed to evaluate whether the range of vibration transmission to targeted anatomic locations during different common activities was effective or not. The test monitored vibration levels experienced at the hip while performing activities described in the labeling for different body types. The

acceptance criteria accounted for the hip acceleration for walking and performing light chores being larger than when the user is standing still. The device met the acceptance criteria.

- **Accuracy testing for accelerometers.**
  A verification test was performed to evaluate whether the accelerometers support the effective use of the device in measuring and delivering appropriate vibrations. The testing consists of mounting the device and a paired hip accelerometer to a cantilevered plate with a calibrated reference accelerometer. The device motor is run at three different Pulse-Width Modulation (PWM) values to capture a range of vibration frequencies and amplitudes. A cantilevered plate was chosen to amplify the vibration measurements to reduce the effect of noise on the accelerometer measurements. Measurements from the Motor and Hip Accelerometers on the device were compared to measurements from the calibration reference accelerometer placed near the motor as acceptance criteria, which was met by the device.

- **Bench testing for safety assessment of strong vibrations**
  A verification test was performed to evaluate the impact on the patient by the strong vibrations which are used for the proposed duration of treatment, specifically addressing the structures immediately surrounding the vibration box. Testing on the safety of the vibration to the hips and spine, with acceptance criteria, was compared against ISO 2631-1 (Ed. 2.0): 1997 + A1:2010, Mechanical vibration and shock – Evaluation of human exposure to whole-body vibration. While this standard is not directly applicable to the Osteoboost Belt because it does not create "whole-body vibration", the specific recommendations are used to set a general vibration safety standard for the design of the Osteoboost Belt along with literature articles supporting the use. In this test, acceptance criteria for the maximum allowable vibration exposure for safety, per ISO 2631-1, was met. Further, the results are also leveraged based on the clinical study and results.

SUMMARY OF CLINICAL INFORMATION

The sponsor conducted a randomized, sham controlled, "triple-blinded" (subject, Principal Investigator and Clinical Research Coordinator, as well as outcomes assessors), prospective, pivotal clinical trial consisting of 126 subjects at a single U.S. site. The study enrolled post-menopausal female subjects older than age 50 years diagnosed with low bone mass (osteopenia) defined by a DEXA T-score between -1.0 and -2.49. The majority of the subject population was Caucasian women (120/126; 95%), with only 6/126 (5%) non-Caucasian subjects.

Enrolled Population	Aged 52-82 Osteopenia (DXA T-score between -1.0 and -2.49) Caucasian women (120/126; 95%), with only 6/126 (5%) non-Caucasian subjects

Excluded Population	• Osteoporotic population • High Fracture Risk Assessment (FRAX) score • Type I Diabetes • Heavy smoking • Severe alcoholic • history of severe renal disease or kidney failure • treated for a herniated disc • BMI > 35
	• Had had a spinal fusion procedure • Had an active implant (e.g., implanted neurostimulator) in the areas of the lumbar or thoracic spine, pelvis, or buttocks • Had had a major change in high-impact physical activity level (increase or decrease) in the past 3 months • Had undergone or was undergoing transgender hormone therapy • Had cancer and/or was being treated for cancer

The primary effectiveness endpoint was a comparison of the mean percentage change in vertebral bone strength between the active and sham treatment groups, as calculated at baseline and 12 months. The surrogate for lumbar vertebral bone strength was based on bone mineral density (BMD). BMD was measured by first lumbar vertebrae (L1) volumetric CT at baseline and at 12 months from which finite element analysis was used to estimate vertebral bone strength. The primary endpoints of BMD and Bone Strength are indirect measures of benefit (not demonstrated to correlate with fractures), and not the endpoints of fracture reduction. Safety was evaluated by adverse events. The sponsor provided 12 months of follow-up on all enrolled subjects.

The results showed that statistical significance, which corresponded to a 0.48% reduction in bone strength for patients who used the device versus an 2.84% reduction in bone strength for patients who used a sham, non-therapeutic version of the device, was only achieved for people who used the device for at least 3 weekly sessions of 24 minutes each (the number of patients who completed the study per protocol was 57.9% (73/126) of those randomized). There were no device-related Serious Adverse Events (SAEs). There were increased incidences of other adverse effects/side effects (e.g., back pain, dizziness, muscle weakness) in the active treatment group as

compared to the sham group; however, these effects were reversible upon cessation of use of the device.

The clinical results indicate minimal risk to post-menopausal osteopenic women (refer to labeling for detailed description of population) when the Osteoboost belt is used as indicated.

LABELING

The labeling includes the following: device description, indications for use, instructions for use, warnings, summary of clinical studies, clinical study population specific warnings, precautions, charging and cleaning instructions, shelf life and disposal instructions, adverse events, side effects and risks. The labeling meets the requirements of 21 CFR 801.109 for prescription devices. The labeling also includes information regarding the limitations of clinical significance of device output, as well as information about the percentage benefit when compared to sham device.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a wearable vibration device for orthopedic use and the measures necessary to mitigate these risks.

Risks to Health	**Mitigation Measures**
Accelerated loss of bone strength and bone mineral density resulting from application of inappropriate magnitude and/or frequency of vibration	Clinical performance testing Non-clinical performance testing Human factors/usability evaluation Software verification, validation, and hazard analysis Electromagnetic compatibility testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Patient injury due to electrical, mechanical, or thermal hazards	Electrical safety testing Electromagnetic compatibility testing Mechanical and thermal safety testing Software verification, validation, and hazard analysis Labeling
Adverse effects on the patient such as regional pain, dizziness, difficulty with balance, headache, nausea, blurred vision, muscle weakness	Clinical performance testing Labeling
User error leading to ineffective reduction in loss of bone strength or bone mineral density	Clinical performance testing Human factors/usability evaluation Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the wearable vibration device for orthopedic use is subject to the following special controls:

(1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must evaluate the reduction in loss of bone strength \or bone mineral density. Testing must evaluate patient risks, including regional pain, dizziness, blurred vision, muscle weakness, difficulty with balance, headache, nausea. The testing should include a broad range (demographics) for at-risk population studied for a minimum of 1 year.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following must be provided:

- (i) Verification and validation of critical performance characteristics of the device, including characterization of the designed outputs of the device as well as the outputs that are delivered to the patient;
- (ii) Non-clinical testing to demonstrate the accuracy, reliability, and reproducibility of device output;
- (iii) Validation that vibration characteristics are within safe physiologic limits; and

(3) The patient-contacting components of the device must be demonstrated to be biocompatible.

(4) Performance data must be provided to demonstrate the electrical safety, basic safety, thermal safety, battery safety, and electromagnetic compatibility of the device.

(5) Software verification, validation, and hazard analysis must be performed.

(6) Labeling must include the following:

- (i) Appropriate patient warnings and precautions associated with the use of the device;
- (ii) A summary of the clinical performance testing with the device, including clinical outcomes and observed adverse events;
- (iii) Information regarding limitations of the clinical significance of the clinical performance data;
- (iv) Identification of the population studied;
- (v) Instructions on duration and frequency of use, and when to discontinue use of the device; and
- (vi) Instructions for device maintenance, including appropriate cleaning of any reusable components and safe disposal of the device.

BENEFIT-RISK DETERMINATION

The probable risks of the device are based on data collected in a clinical study described above.

There were no observed device-related SAEs. However, the adverse events associated with the use of the device were observed more frequently in the active treatment group than in the sham group. The most common adverse events were related to dizziness, lower or upper back pain, muscle weakness, leg or pelvic pain, tenderness or bruising at site of application and adverse skin reactions. However, it is noted that the observed adverse events/side effects/risks of the device were reversed with cessation of use of the device.

The probable benefits of the device are also based on data collected in a clinical study as described above.

The primary endpoints of reduction in the loss of BMD and Bone Strength are indirect measures of benefit and do not constitute direct endpoints of fracture reduction. The marginal statistical benefit observed between the active and sham groups (who used the device as indicated) show that the treatment group lost 0.48% of vertebral bone strength compared to a 2.84% loss in the sham group, while the treatment group lost 0.29% of their volumetric BMD compared to 1.97% in control subjects. Therefore, the difference of 2.36% in the decline of vertebral bone strength and the difference of 1.68% in the decline of volumetric BMD are considered as statistical benefit for this device. It should be noted that the endpoints used (vBMD and Bone Strength), while not direct assessments of fractures (i.e., the evidence supporting probable clinically relevant benefit is uncertain), are nonetheless important parameters that can impact fracture risk assessment.

Some additional factors that impact the device's benefit-risk profile are related to the population evaluated in the clinical study of the device. In the study of the device, a high majority of the evaluated patients were Caucasian, and non-Caucasian populations were underrepresented. Therefore, the clinical benefits of using the device in non-Caucasian populations have not been extensively demonstrated. Evaluated patients also lacked high risk factors for developing bone fragility such as heavy smoking, type I diabetes, history of fractures, or renal disease. Furthermore, subjects with a BMI >35 were not evaluated. The clinical benefit of the device (statistical benefit of 2.36% bone strength and 1.68% of BMD) is only observed for subjects who used the device per protocol.

This device is not indicated for patients with osteoporosis.

The device is a prescription use device with low risks (adverse events/side effects) that are reversible upon cessation of use of the device and demonstrated clinical benefit in slowing the age-related progressive loss of bone strength and bone mineral density in postmenopausal women with osteopenia.

Patient Perspectives

The low number of subjects completing the study per protocol, raises concerns towards the compliance of the device while using it. However, the low sample size was attributed to non-device related reasons. Further, results from a patient preference survey were provided.

Patient perspectives considered for the Osteoboost Belt during the review include information that captures relative acceptability of outcomes and favorable response in using the device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The Osteoboost Belt is indicated to reduce the decline in bone strength and volumetric bone density, as assessed via CT scans that were analyzed using the VirtuOst estimate of vertebral bone strength and density in postmenopausal women with osteopenia of the lumbar vertebrae or total hip as diagnosed via DXA with a BMD T-score between -1.0 and -2.49.
>
> - The clinical effects have only been observed for the duration of the clinical study performed to support the indications for use (1 year).
> - Fracture risk was not evaluated in the clinical study to support the indications for use, so it is not known how the treatment effects correlate with fracture risk.
> - The clinical effects have been demonstrated only for those who used the device as indicated.

The probable benefits outweigh the probable risks for the Osteoboost Belt. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Osteoboost Belt is granted and the device is classified as follows:

> Product Code: QZO
> Device Type: Wearable vibration device for orthopedic use
> Regulation Number: 21 CFR 888.5895
> Class: II