DE NOVO CLASSIFICATION REQUEST FOR

SONU

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **External mechanical stimulator for the relief of congestion**. An external mechanical stimulator for the relief of congestion delivers vibrations to the sinus and nasal areas to relieve congestion.

NEW REGULATION NUMBER: 21 CFR 874.6010

CLASSIFICATION: Class II

PRODUCT CODE: QZC

BACKGROUND

DEVICE NAME: Sonu

SUBMISSION NUMBER: DEN230045

DATE DE NOVO RECEIVED: June 16, 2023

SPONSOR INFORMATION:

Sound Health Systems, Inc.
% Sloan Regulatory Consulting, LLC
322 Hart Rd.
Gaithersburg, Maryland 20878

INDICATIONS FOR USE

The Sonu is indicated as follows:

> Sonu is indicated for the relief of moderate to severe nasal congestion due to allergic and non-allergic rhinitis. Sonu is a treatment to be used at home by individuals 22 and older.

LIMITATIONS

Limitations on device use are included in the Instructions for Use as Contraindications, Warnings, and Precautions.

Contraindications

You should not use this device if:

• You have a dental infection.

• You are receiving treatment for neurological conditions.

• You have electrostimulation devices implanted in your head, including a deep brain stimulation (DBS) devices or cochlear implants

• You had any type of surgery to the face, head, nose or sinuses within the past 3 months

• You had an intracranial or and intracerebral bleeding in the past 6 months.

• You have open wounds, rashes, over swollen, red, infected or inflamed areas, skin eruptions or fragile skin on the forehead (treatment location).

• You have a history of cranial surgery.

• You are sensitive to sound.

Precautions

• Congestion relief for greater than 2 weeks has not been studied.

• Do not attempt to perform any treatment before carefully reading this User Manual and Quick Start Manual provided with the package.

• Do not use the device on the heart, chest, neck, or any other body location other than the forehead as directed.

• Do not share the device with other people. The device is intended to be used by a single person to receive therapy based on their craniofacial anatomy.

• Refer to Sound Health Systems' website: https://soundhealth.life for detailed information.

Warnings

Sonu transmits acoustic vibrations from the bone conduction transducers in the Band to the sinus cavities. After you pair the Band with your smartphone and play the audio track, you will hear sound during treatment (essential performance).

• Do not use Sonu if you are unable to pair the Band with the Sonu App on your smartphone or do not hear sound when you play the audio track (i.e., essential performance is lost or degraded) due to electromagnetic disturbances.

• Do not use Sonu if it shuts down or the performance has degraded in any way

• Do not use Sonu near active high-frequency (HF) surgical equipment or in the radiofrequency (RF) shielded room of a magnetic resonance imaging (MRI) scanner or near RF emitting equipment where electromagnetic disturbances are high, because it could result in improper operation.

• Avoid using Sonu adjacent to or stacked with other equipment because it could result in improper operation. If such use is necessary, please verify that Sonu and the other equipment are operating normally.

• Use of accessories, transducers and cables other than those specified or provided by the manufacturer of Sonu could result in increased electromagnetic emissions or decreased electromagnetic immunity of Sonu and result in improper operation.

• Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of Sonu, including cables specified by the manufacturer. Otherwise, degradation in performance of Sonu could result.

DEVICE DESCRIPTION

Sonu is a non-invasive, over-the-counter (OTC) device designed for the relief of moderate to severe nasal congestion due to allergic and non-allergic rhinitis at home. Sonu consists of an adjustable headband (Sonu Band) with integrated acoustic bone-conduction transducers, a USBC Charging Cable, and a smartphone application (Sonu iOS App) that connects to the Sonu Band.

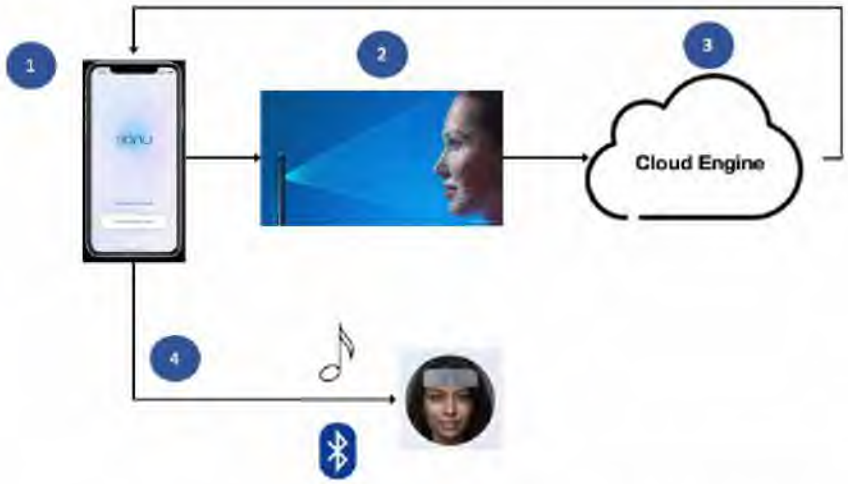
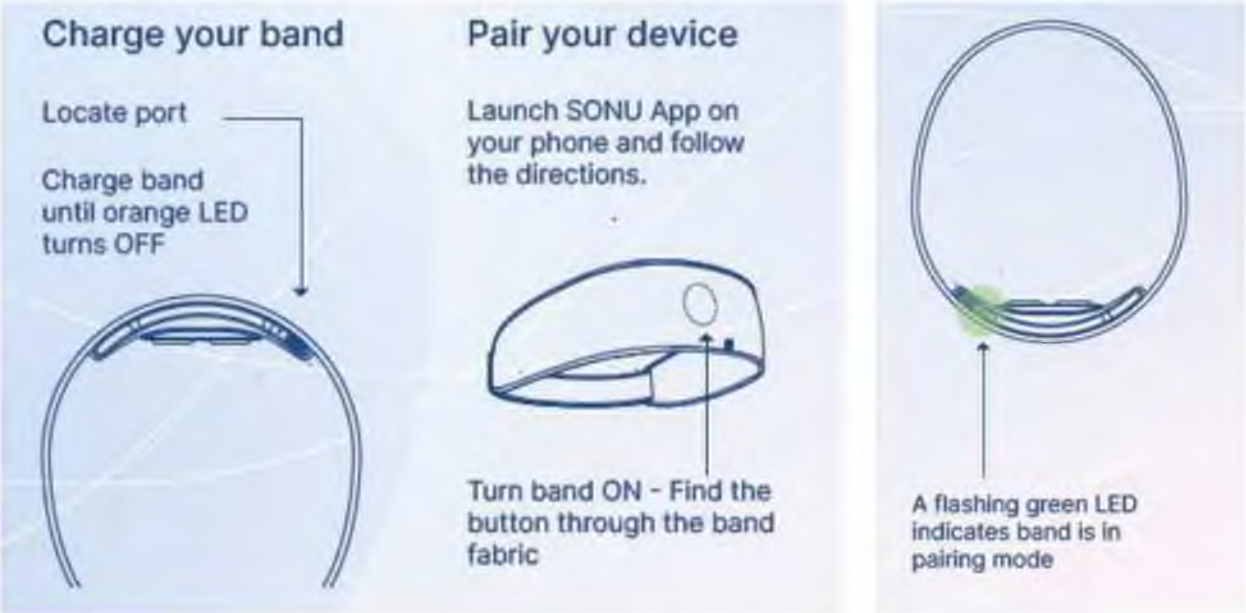


Figure 1. Sonu Components and Modes of Interaction

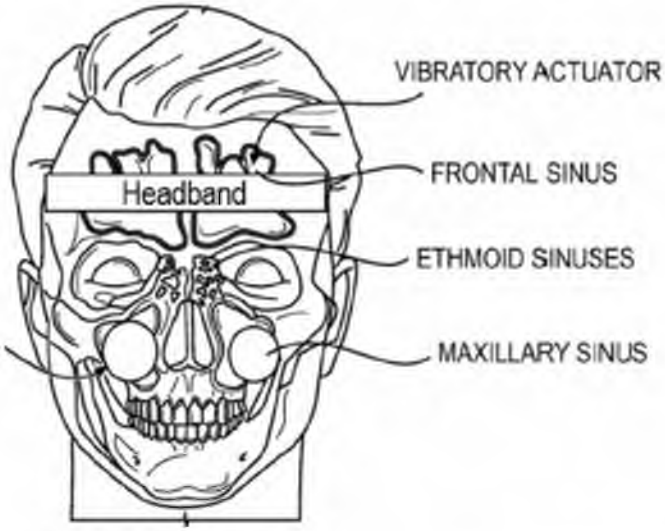
The following describes each of the numbered components and interactions shown in Figure 1:

1. **Sonu iOS App**: The user downloads the Sonu App on their iOS-based smartphone and is guided through a simple setup process. This process involves Bluetooth pairing of the Sonu Band to the smartphone and follows the standard secure procedure to pair a headphone device via Bluetooth.



2. **3D Face Scan**: The Sonu App directs the user to perform a detailed 3D face scan using the front-facing smartphone camera and calculates vector distances for selected craniofacial landmarks based on the 3D scan. These vector values are then encrypted and sent to the Sonu Cloud Engine over wireless air interface. Note: No photos or user facial scans are stored on the smartphone or sent to the Sonu Cloud Engine to ensure complete compliance with user privacy.

3. **Sonu Cloud Engine**: The Sonu Cloud Engine estimates patient-specific resonant frequencies of nasal cavities and sinuses (using an Artificial Intelligence / Machine Learning algorithm that has been trained to correlate craniofacial measurements with sinus dimensions) and sends the Sonu App instructions to sequence and play them (deliver treatment), as an audio file, via the Sonu Band.



4. **Treatment Delivery via Bluetooth-paired Sonu Band**: The Sonu App then synthesizes, sequences, and plays the audio file through the Sonu Band's acoustic bone conduction transducers to deliver patient-specific treatment. Each dose consists of a 15-minute playback sequence. The recommended treatment is two doses per day for relief of congestion.

The acoustic energy levels of the Sonu Band are below that specified by the World Health Organization (WHO) for safe headphone operation for the maximum dosage period (< 88 dB SPL) in "Safe Listening Devices and Systems_WHO-ITU Standard H.870

Clinical studies have shown that acoustic energy or vibration results in nasal decongestion.[7,8,9,10] Specific breathing exercises that incorporate humming have been practiced for centuries and have recently been demonstrated to reduce symptoms of chronic sinusitis including nasal congestion.[11,12] A single-frequency vibrational device with positive pressure was recently shown

to have beneficial effects on patients with chronic nasal congestion without fixed anatomic obstruction.[13,14] Vibration is thought to decrease congestion through three possible mechanisms (a) sino-nasal mucosal vasoconstriction, (b) increased muco-ciliary clearance, and (c) decreased mucus viscosity. Vibration has also been shown to result in vasoconstriction in vivo.[15,16,17] In patients with chronic pulmonary disease, techniques using vibration have been shown to increase muco-ciliary clearance.[17,18,19] Mechanical oscillations on non-Newtonian fluids like mucus, have been shown to decrease viscosity.[17,20]

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[8] Maniscalco M, Pelaia G, Sofia M. Exhaled nasal nitric oxide during humming: Potential clinical tool in sinonasal disease? Biomark Med. 2013;7(2):261–6.
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[11] Abishek K, Bakshi S, Bhavanani A. The efficacy of yogic breathing exercise Bhramari pranayama in relieving symptoms of chronic rhinosinusitis. Int J Yoga. 2019;12(2):120.
[12] Phillips KM, Roozdar P and Hwang PH, Applications of vibrational energy in the treatment of sinonasal disease: A scoping overview, Int. Forum Allergy Rhinol., 2022; 12: 1397-1412. https://onlinelibrary.wiley.com/doi/full/10.1002/alr.22988
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[19] Wanner A, Salathé M and O'Riordan TG, Mucociliary clearance in the airways. American Journal of Respiratory and Critical Care Medicine 1996; 5: 868–902.
[20] Obembe AD, Roostaie M, Boudreault R and Leonenko Y, On the effect of boundary vibration on mucus mobilization, Int. J. Non-Linear Mech. 2022; 142: 104019. https://doi.org/10.1016/j.ijnonlinmec.2022.104019

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Sonu Band has a "cut out" in the fabric to allow contact of the transducers (which are covered by medical grade silicone rubber (b)(4) covers) with the forehead as shown in Figure 1 below:

Figure 1. Inner Surface of Sonu Headband Showing Medical-Grade Silicone Transducer Covers

As shown in the table, only the inner headband and transducer covers have direct contact with intact skin; all other components do not contact the patient. The nature of contact is on "intact skin" for limited (< 24 hours) duration. As stated in Section IV(A) of FDA's guidance, "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process," (issued September 8, 2023) "some devices are made of materials that have been well characterized both chemically and physically in the published literature and/or have a long history of safe use in legally US marketed medical devices. It may not be necessary to conduct testing for all or a portion of the biocompatibility endpoints suggested in the FDA matrix of this guidance."

Component	Material	Patient Contact?
Transducers	(b)(4)	No
Transducer, Battery and Printed circuit board cases; End caps		No
Double-sided Tape		No
Light-Emitting Diode (LED) Light Guide		No
Microphone Gasket, Bridges		No
Battery Tape		No
Front Cover		No
Guard (Inside pad for button)		No
Adhesives		No
Lock Screws		No
Headband (Outer)		No
Headband (Inner)	Polyester (PET); (b)(4) polyurethane ((b)(4))	Direct contact with intact skin
Transducer Covers	Medical grade silicone rubber (b)(4) [in two color options: none (translucent) and purple]	Direct contact with intact skin

The PET, polyurethane, and silicone that compose the inner headband and transducer covers are listed in Attachment G of FDA's guidance as materials which "pose a very low biocompatibility risk because they have a long history of safe use in medical devices that contact intact skin." FDA further states in this attachment that this policy "describes a least burdensome approach for these devices that recommends specific material information to be included in a premarket submission in lieu of biocompatibility testing." Sonu meets all the characteristics outlined in the policy: it is a medical device contacting intact skin surface only, has a limited contact duration, and is composed on materials outlined in Section B of Attachment G.

Furthermore, none of the exclusion characteristics listed in the guidance apply to the device:
- The PET, polyurethane, and medical grade silicone composing the inner headband are explicitly included in the list of synthetic polymers with very low biocompatibility risk,

- The inner headband is not stored in or does not contain fluids or creams,
- The inner headband is not fabricated from in-situ polymerizing materials, absorbable materials, or hydrogels,
- The inner headband does not contact breached or compromised surfaces, as abraded or shaved skin, or open or healing wounds,
- The inner headband is not a reprocessed single-use device,
- The inner headband does not include adhesives to attach the device directly to the skin.

Finally, A statement describing how biocompatibility risks are addressed in the Device Master Record (DMR), which addresses concerns identified through manufacturing information (based on the type of materials, formulation, available information on the materials, and nature of contact), and relevant quality system requirements and post-market controls related to:
- Purchasing controls (21 CFR 820.50) of device materials,
- Production and process controls (21 CFR 820.70) for manufacturing materials,
- Acceptance activities (21 CFR 820.80) for component and manufacturing materials,
- Corrective and preventative action (21 CFR 820.100),
- Complaint files (21 CFR 820.198), and
- Medical device reporting (MDR) (21 CFR 803).

SHELF LIFE/STERILITY

Sonu components are provided non-sterile given their intended use as either contacting intact skin only (Sonu Band) or non-contact (USB charging cable). Therefore, no sterilization information is required. Sonu packaging, transit, and shelf-life testing was completed. Test results support labeling the device for a shelf life of 12 months.

ELECTROMAGNETIC CAPABILITY & ELECTROMAGNETIC SAFETY

EMC tests for a Group 1 Class B medical device intended for the home healthcare environment were conducted on Sonu by SGS Taiwan Ltd. (No.2 Keji 1st Rd., Guishan District, Taoyan City, Taiwan) to the following standards:

• IEC 60601-1-2 (Edition 4.0): 2014+AMD1:2020.
• 47 CFR FCC Part 15 Subpart B (Class B), ANSI C63.4: 2014

The following tests were conducted with results summarized in the sections below.
• IEC 60601-1-2 Referenced Emission and Immunity Standards
• Conducted and Radiated Emissions
• Radiofrequency (RF) Exposure
• Electromagnetic Emissions
• Battery Safety

Per the above testing, Sonu is electromagnetically compatible, electrically safe, and has a safe battery for its intended use.

SOFTWARE

Sonu incorporates software for its designed user interface and device treatment functionality (via a Smartphone App). Information was provided based on FDA Guidance "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 11, 2005":

Software Documentation (per FDA Guidance)	Description
Level of Concern	Minor Level of Concern (LOC)
Software Description	Summary overview of the features and software operating environment.
Device Hazard Analysis	Tabular description of identified hardware and software hazards, including severity assessment and mitigations.
Software Requirements Specification (SRS)	Summary of functional requirements from SRS.
Traceability Analysis	Traceability among requirements, specifications, identified hazards and mitigations, and Verification and Validation testing.
Verification and Validation Documentation	Software functional test plan, pass/fail criteria and results.
Revision Level History	Revision history log, including release version number and date.

Sonu was also assessed regarding cybersecurity taking into consideration FDA's guidance, "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices" (October 2014).

PERFORMANCE TESTING - BENCH

Functional Testing of the Sonu Band was conducted. All devices were inspected and 100% tested for functionality after manufacturing. Results of functionality testing of finished Sonu Bands are provided below. All (60 of 60) units passed battery and functional pairing tests. Four (4 of 60) units had minor cosmetic defects (burr, sink marks, marker alignment). A non-conformance report was generated; the units were examined and deemed acceptable by Sound Health Systems.

Operation	Work Instructions	Quality/Inspection Criteria	Inspection Methods	Results
Test charging and battery connectivity functionality	Charge the band via USB to verify charging connection	Charging indicator must turn on. and achieve next level of charge	Manual / Visual	100% Passed
Test unit and phone pairing functionality	Pair the headband with an iPhone X via Bluetooth and verify pairing functionality; Follow Sonu pairing instructions.	Band must be paired successfully with iPhone X	Manual / Visual	100% Passed
Test audio quality and volume	Audio quality: Download App on iPhone. Follow App directions and "measure" therapeutic resonance. Volume control: Play track at "max" and "50% volume" settings and verify corresponding volume changes. Maximize the band volume by pushing the '+' button on the bottom of the band until a short set of double (2) beeps are heard. This denotes the "max" scale. Verify that the sound increases appropriately.	Verify that therapeutic resonance is measured. Verify that volume changes at "max" and "50% volume" settings.	Manual / Visual	100% Passed

The results of bench testing demonstrate that Sonu performs as intended.

PERFORMANCE TESTING - ANIMAL AND/OR CADAVER

No animal testing was performed, nor is required, to demonstrate the intended function or safety of the device. A preliminary version of the device (Soniflow System) was evaluated in a human cadaver model to verify the resonance frequency calculation algorithm.

SUMMARY OF CLINICAL INFORMATION

The SCORE (Sonu nasal COngestion RElief) Study was a multi-center, randomized, double blinded, sham-controlled (Sonu versus Sham, randomized 1:1), interventional study of 52 subjects. The study was designed to assess the safety and effectiveness of acoustic resonance therapy as delivered through the Sonu Band in subjects suffering from moderate to severe nasal congestion due to allergic and non-allergic rhinitis. Three (3) sites participated in the study.

Subjects who met the inclusion/exclusion criteria were invited to participate in the study:

Inclusion Criteria:
- 18 years of age or older
- Symptoms of nasal congestion for 1 month or more
- Have a 24-hour reflective nasal congestion sub-score of the Total Nasal Symptoms Score (TNSS) of 2 or more on a 0 to 3 scale at the time of screening

Exclusion Criteria:
- Head, nasal or sinus surgery within 3 months
- Sinus infection diagnosed within the last month, or rhinitis medicamentosa
- Documented history of nasal polyposis or mass

Subjects were instructed on use of Sonu by study staff. Subjects were advised to self-perform the treatment at home twice a day for 2 weeks. Subjects were provided the Quick Start Manual with an on-line link to the detailed User Manual. Subjects were sent notifications by the software to use Sonu twice a day for 2 weeks.

Subjects were 1:1 randomized to the following cohorts:
- Active Treatment: Sonu Therapy for 15 minutes, twice a day
- Sham: Non-resonant acoustic energy (2 kHz, 2 second duration tone every 10 seconds at 50% volume) for 15 minutes, twice a day.

Subjects reported their nasal congestion sub-score and 24-hour reflective TNSS at baseline and after their second treatment each day on the Sonu App. The nasal congestion sub score is part of the TNSS, a validated symptom severity scoring system (*Downie SR, Andersson M, Rimmer J, Leuppi JD, Xuan W, Akerlund A, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. Allergy Eur J Allergy Clin Immunol. 2004;59(4):406–14*). The nasal congestion sub-score is evaluated using a scale of 0=None, 1=Mild, 2=Moderate, or 3=Severe.

Primary Safety Endpoint: Serious Adverse Events
Primary Safety as defined as a lack of serious adverse events (SAEs, defined as any untoward medical occurrence in a subject, regardless of whether the event is related to the device that):
a. results in death;
b. results in a life-threatening illness or injury;
c. results in a permanent impairment of a body structure or body function;
d. requires in-patient hospitalization or prolongation of existing hospitalization;
e. results in medical or surgical intervention to prevent permanent impairment to body structure or function;
f. results in fetal distress, fetal death, or a congenital abnormality/birth defect.

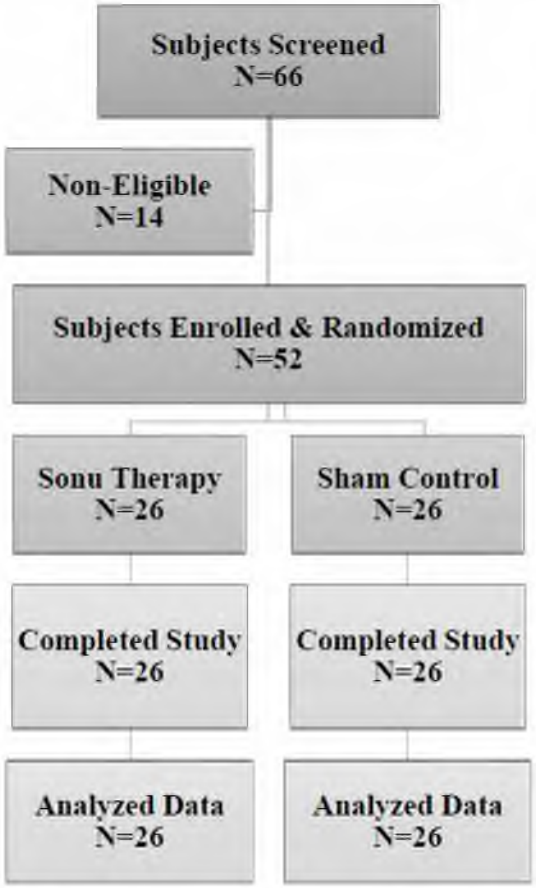
Primary Effectiveness Endpoint
Primary effectiveness as defined by a statistically significant improvement in nasal congestion sub-score of TNSS, comparing baseline congestion at screening versus daily congestion averaged over 2 weeks (Sonu vs. Sham).

Secondary Safety Endpoint: Adverse Events

Safety as defined as a lack of adverse events (AEs). AEs were defined as any untoward medical occurrences in a subject, regardless of whether the events were related to the device.

Secondary Effectiveness Endpoint

Secondary effectiveness as defined by a statistically significant improvement in 24-hour reflective TNSS comparing baseline TNSS at screening versus daily TNSS averaged over 2 weeks (Sonu vs. Sham).



The SCORE study enrolled and randomized 52 subjects (26 Sonu Therapy and 26 Sham) from three (3) centers, with broad representation of patients with both allergic and non-allergic rhinitis. consort diagram of eligible subjects screened and enrolled is shown below. There was a slight gender skew in enrollment favoring males, but this was statistically adjusted in all outcomes analyses. Subjects were highly adherent with 84.8% of possible treatment doses initiated (1234 doses out of a total possible of 1456 doses). Adherence was similar between two groups with 81.0% (95% CI 71.1%, 91.0%) in the Sonu Therapy group vs. 88.5% (95% CI 83.3%, 93.6%) in the Sham (p=0.18). Blinding was satisfactory, as determined by Bang's blinding index of -0.08 for our sham arm, and slightly higher (0.36) for the active treatment arm.

Table 1 Subject Demographics

	Sonu Therapy	Sham	Total	p-value
Sex				
Male (%)	16 (61.5%)	6 (23.1%)	22 (42.3%)	0.005
Female (%)	10 (38.5%)	20 (76.9%)	30 (57.7%)	
Age Mean ± Standard Deviation Median (minimum-				
Mean ± Standard Deviation	45.3 ± 17.7	48.8 ± 14.9	47.1 ± 16.3	0.38
Median (minimum-maximum)	43.5 (18-76)	48 (18-72)	45 (18-76)	
Ethnicity*				
Hispanic/Latino	6 (23.1%)	4 (15.4%)	10 (19.2%)	0.48
Not-Hispanic/Latino	20 (76.9%)	22 (84.6%)	42 (80.8%)	
Race*				
Asian	6 (28.6%)	4 (18.2%)	10 (23.3%)	0.45
Unknown	0 (0.0%)	1 (4.5%)	1 (2.3%)	
White	14 (66.7%)	17 (77.3%)	31 (72.1%)	
White/Asian	1 (4.8%)	0 (0.0%)	1 (2.3%)	
Allergic vs. Non-Allergic Rhinitis				
Allergic (%)	12 (48.0%)	16 (61.5%)	28 (54.9%)	0.33
Non-Allergic (%)	13 (52.0%)	10 (38.5%)	23 (45.1%)	
Baseline Nasal Congestion Sub-score				
Mean ± Standard Deviation	2.27 ± 0.45	2.12 ± 0.33	2.20 ± 0.39	0.17
Baseline TNSS Mean ± Standard Deviation	6.65 ± 2.37	6.58 ± 2.10	6.62 ± 2.24	0.9
Medication				
Subjects on Daily Allergy meds during treatment	10/26 (38.5%)	13/26 (50.0%)	23/52 (44.2%)	0.4

Primary Safety

The primary safety endpoint was achieved based on the absence of any reported Serious Adverse Events (Table 3). Furthermore, there were no reports of any adverse events or complications related to the device or treatment.

Table 3. Serious Adverse Events

Total Subjects / Total Treatments	Device or Procedure-Related SAEs
52 Subjects / 1234 Total Treatments	0

Primary Effectiveness Analysis - Nasal Congestion Sub-score

The primary effectiveness endpoint was achieved, based on the statistically significant reduction in the nasal congestion sub-score in the Sonu Therapy arm compared to Sham. At 2-week follow-up, the mean change in nasal congestion sub-score was -0.87 in the Sonu Therapy group and -0.44 in the Sham group (p=0.008). **Figure 3** shows the average change in nasal congestion sub-score for the Sonu Therapy (Group A) and Sham (Group B) groups. After adjustment for age, gender and allergic/non-allergic rhinitis, the difference in change of nasal congestion sub-score between two groups increased from 0.43 to 0.47 (95% confidence interval (CI) 0.15, 0.79) and remained statistically significant (p=0.005).

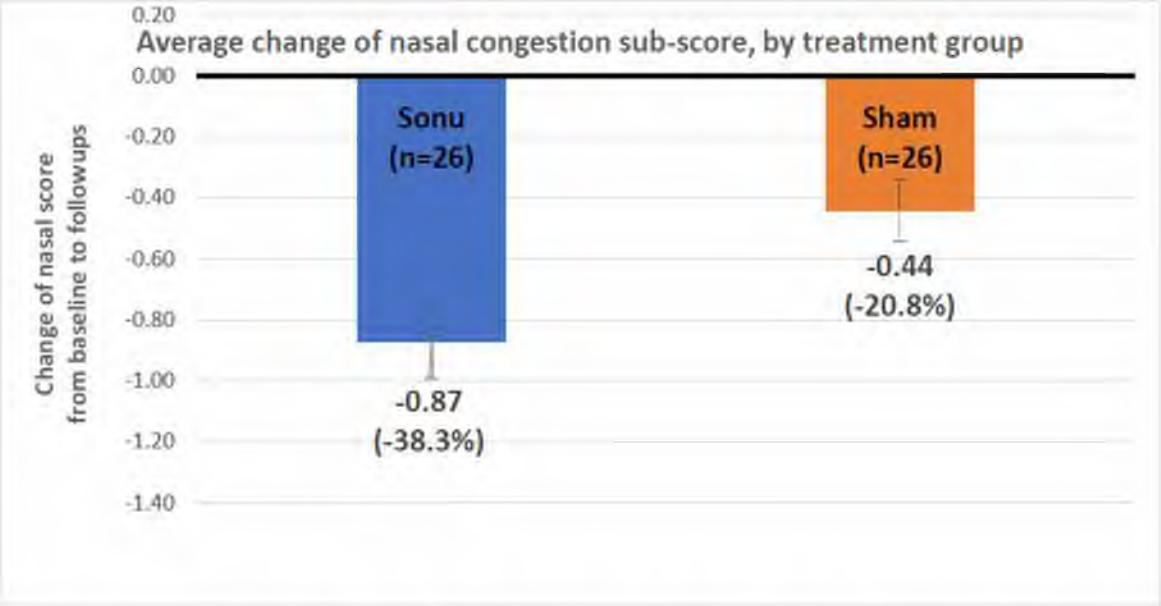


Figure 3. Mean Change in Nasal Congestion sub-score with standard error, by group

Outcome data for the primary and secondary effectiveness endpoints are summarized below:

Study Outcomes for Nasal Congestion Sub-score and TNSS

	Mean Change from Baseline (95% CI)				
	Sonu Therapy		Sham		
	Mean change	95% CI	Mean change	95% CI	p-value
Primary Endpoint - Nasal Congestion Sub-score	-0.87	-1.11, -0.62	-0.44	-0.64, -0.23	0.008
Secondary Endpoint - Composite TNSS	-2.85	-3.85, -1.85	-1.32	-2.27, -0.36	0.027

TNSS = Total Nasal Symptom Score; CI = confidence interval

Nasal Congestion Sub-Score - Week 1 and Week 2

A time analysis was performed comparing weekly average nasal congestion sub-scores for Sonu Therapy vs Sham at baseline compared to Week 1 and Week 2 of treatment, as shown in **Figure 4**. The nasal congestion sub-score continued to improve in Week 2 compared to Week 1. The nasal congestion sub-score decreased by 33% in Week 1 and 44.5% in Week 2 for Sonu Therapy compared to only 20.3% in week 1 and 19.3% in Week 2 for Sham. For Sonu Therapy vs Sham, the decreases were already statistically significant by Week 1 (p=0.030) and continued to be significant in Week 2 (p=0.008). Using repeated measures analysis, the between-group difference in reduction in nasal congestion sub-score was 0.49 (95% CI 0.06, 0.92, p=0.026) at day 14, exceeding the difference obtained using the 14-day average of 0.43 (95% CI -0.12, 0.74, p=0.008).

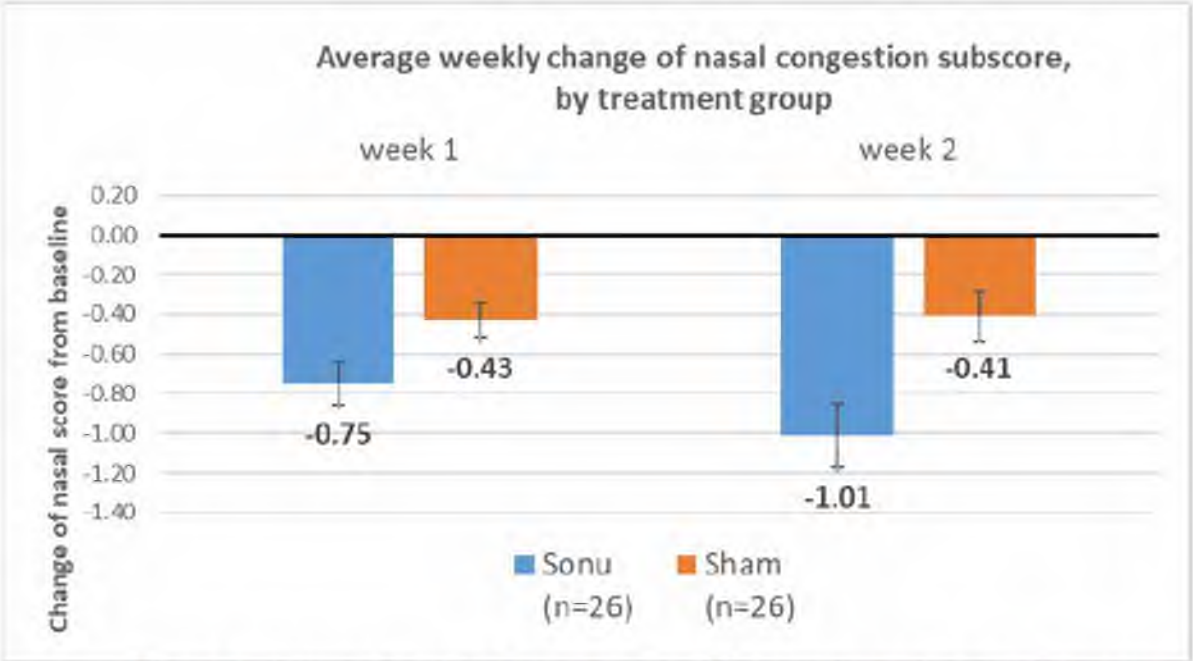


Figure 4. Average weekly change in Nasal Congestion sub-score, by group

Secondary Safety

The secondary safety endpoint was achieved based on the absence of any reported Adverse Events (Table 4).

Table 4. Adverse Events

Total Subjects / Total Treatments	Device or Procedure-Related AEs
52 Subjects / 1234 Total Treatments	0

Secondary Effectiveness Analysis – Total Nasal Symptom Score (TNSS)

TNSS is a validated symptom severity scoring system consisting of the sum of four (4) individual subject-assessed symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing, each evaluated using a scale of 0-3. The TNSS has a maximum possible score of 12. The subject assessment was based on the symptom severity prior to intervention with the study device.

For composite TNSS, the mean change at 2-week follow-up was -2.85 for the Sonu Therapy group and -1.32 for the sham group (p=0.027), as shown in Figure 5. After adjustment for age, gender and allergic/non-allergic rhinitis, the difference in change of TNSS between two groups increased from 1.53 to 1.80 (95% CI 0.46, 3.13) and remained statistically significant (p=0.009). See Table 5 for data summary for primary and secondary outcomes and Figure 6 for Week 1 and Week 2 data. Using repeated measures analysis, the unadjusted difference between groups for the reduction in TNSS was 1.77 (95% CI 0.45, 3.09, p=0.009) at day 14; the adjusted difference between groups for the reduction in TNSS was 2.16 (95% CI 0.80, 3.53, p=0.002) at day 14. Both measures exceeded the difference obtained using the 14-day average shown above.

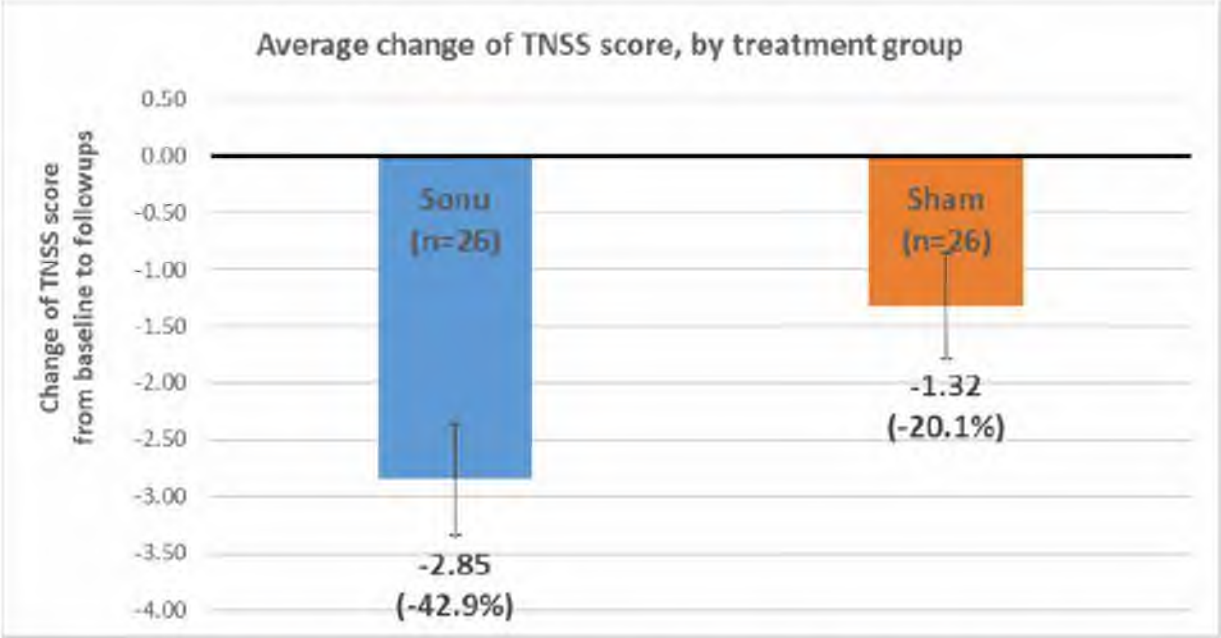


Figure 5. Mean Change in TNSS with standard error, by group

TNSS – Week 1 and Week 2

A time analysis was performed comparing weekly average TNSS for Sonu Therapy vs Sham at baseline compared to Week 1 and Week 2 of treatment, as shown in **Figure 6**. The TNSS continued to improve in Week 2 compared to Week 1. The TNSS decreased by 2.53 (38%) in Week 1 and 3.33 (50.1%) in Week 2 for Sonu Therapy compared to only 1.33 (20.2%) in Week 1 and 1.48 (22.5%) in Week 2 for Sham. For Sonu Therapy compared to Sham, the decreases did not quite meet statistical significance by Week 1 (p=0.065) but reached statistical significance by Week 2 (p=0.02).

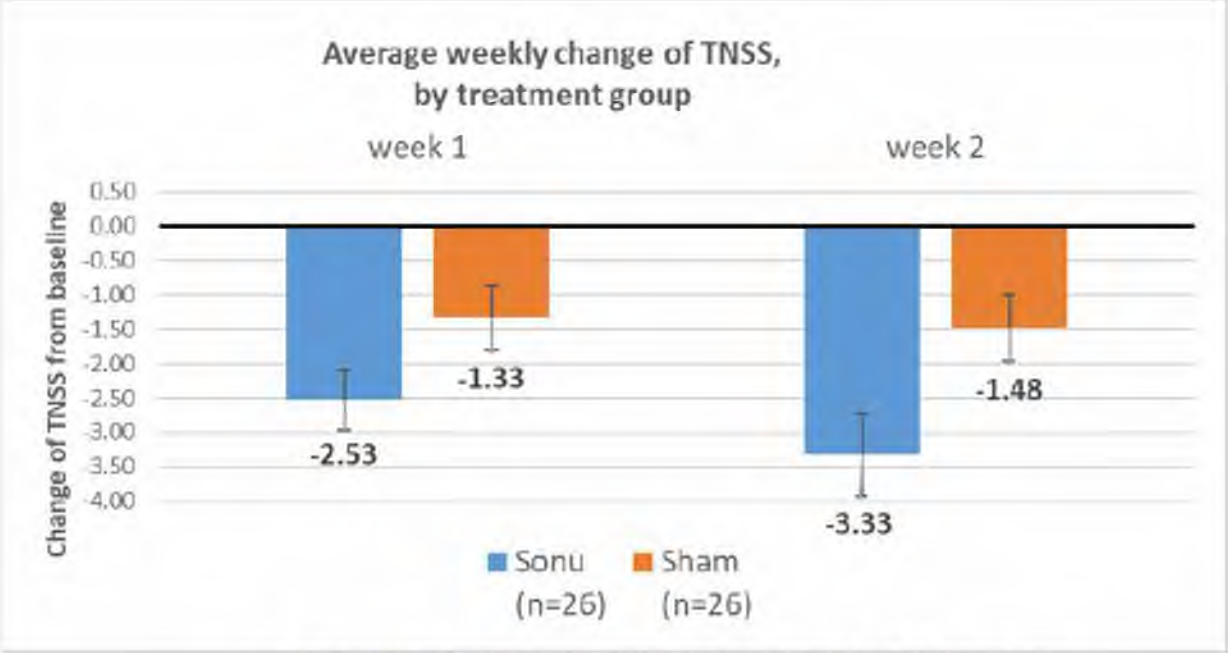


Figure 6. Average weekly change in TNSS, by group

Allergic and Non-Allergic Subgroup Analysis

Both the allergic and non-allergic subjects showed greater reductions in TNSS and nasal congestion sub-scores compared to sham (baseline vs. 2-week average). These differences were only statistically significant for the non-allergic subgroup for nasal congestion (baseline vs. 2-week average, p=0.012). The difference was also statistically significant for the allergic subgroup for TNSS (baseline vs. 2-week average, p=0.008). Although the study was not powered to assess differences in these subgroups, further analysis showed a statistically significant difference in the nasal congestion sub-score at Day 11 and 12 for the AR subgroup. It is believed that a statistically significant change for AR would have been achieved with a larger sub-group. The overall effect size for the AR group at two weeks is 0.38 (p=0.11), which was just slightly below the overall statistically significant effect size of 0.44 for all 52 patients (p=0.008).

CONCLUSIONS

Based on the two-week, multi-center, randomized, double blind, sham-controlled interventional

study of 52 subjects (26 Sonu and 26 Sham) suffering from moderate to severe nasal congestion from allergic and non-allergic rhinitis, the following conclusions can be made:
• Acoustic resonance therapy (ART) using Sonu was safe with no adverse events reported.
• Sonu significantly reduced nasal congestion compared to Sham (-0.87 vs -0.44, p=0.008).
• Sonu significantly reduced TNSS compared to Sham (-2.85 vs -1.32, p=0.027).

In conclusion, the results from this clinical study report demonstrate that Sonu is safe and effective for use at home for the treatment of moderate to severe nasal congestion in subjects with allergic and non-allergic rhinitis.

Pediatric Extrapolation
In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The SONU labeling is sufficient and meets labeling requirements for over-the counter devices. It contains the indication for use, limitation, contraindication, device description, maintenance, warning, caution, instruction for use, summary of clinical trials, information related to electromagnetic compatibility, expected device life, environmental operating conditions, electrical specifications, and symbols and markings.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of the external mechanical stimulator for the relief of congestion and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Injury from mechanical overstimulation on the face causing one or more of the following: • Skin irritation or redness • Pain • Discomfort • Headache • Vertigo • Hearing loss • Tinnitus	Non-clinical performance testing Human factors testing Software verification, validation, and hazard analysis Electrical safety testing Electromagnetic compatibility testing Battery safety testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Ineffective treatment leading to worsening congestion	Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the external mechanical stimulator for the relief of congestion is subject to the following special controls:

Special Controls
(1) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including verification of specified mechanical stimulation parameters. (2) Performance data must demonstrate the electromagnetic compatibility, battery safety, and electrical safety of the device. (3) Software verification, validation, and hazard analysis must be performed. (4) The patient-contacting components of the device must be demonstrated to be biocompatible. (5) Human factors testing must demonstrate that users can successfully use the device in the intended use environment based solely on its labeling and instructions for use. (6) Labeling must include the following: a. Device specifications, including the frequency range, maximum output power, and power source; b. Explanations of the user-interface.

BENEFIT-RISK DETERMINATION

The risks of the device are based on nonclinical bench tests as well as data collected in the clinical study described above.

Nonclinical bench tests were based on performance criteria derived from user needs, resulting product specifications and risk analysis (i.e., Design Failure Modes and Effects Analysis (DFMEA)), as well as consideration of applicable standards. For instance, volume changes were verified at "max" and "50% volume" settings to prevent mechanical overstimulation, and to ensure that energy levels of the Sonu Band were below that specified by the World Health Organization for safe headphone operation for the maximum dosage period (< 88 dB SPL) in "Safe Listening Devices and Systems_WHO-ITU Standard H.870

There were two clinical studies evaluating the safety of the device. The first was an open-labeled study with a previous version of the device in which 50 subjects used the device for two 10-minute sessions over one day. There were no adverse events (AEs) or severe adverse events (SAEs) reported. The second clinical study (SCORE, described above in the SUMMARY OF CLINICAL INFORMATION) was a multi-center, randomized, double blinded, sham- controlled study (Sonu [n=26], sham [n=26]) in which subjects used the device two 15-minute sessions twice a day for 2 weeks. There were no AEs or SAEs reported. There has not been a study past 2 weeks duration. Therefore, it is unclear if there could be risks with repeated use past 2 weeks. To reconcile this, the following was added to the User Guide (labeling): "*3.3. Precautions*
•*Congestion relief for greater than 2 weeks has not been studied.*"

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

The use of vibration was proposed to potentially decrease congestion through three possible mechanisms:
(i) sino-nasal mucosal vasoconstriction,
(ii) increased muco-ciliary clearance,
(iii) decreased mucus viscosity.

A study was provided in which the treatment with the device (as intended) is compared to a sham treatment. The study demonstrated a greater reduction in nasal congestion sub-score compared to the sham treatment. In addition, in a previous open-labeled study of an earlier version of the device, the device did exceed a sponsor defined, minimal clinically important difference (MCID).

The sponsor provided an acceptable rationale for the minimal clinically important difference. The primary endpoint results met and exceeded the MCID. Although for the subgroup of allergic rhinitis (AR) patients in the product arm did not demonstrate a statistically significant difference in improvement to the sham arm, there was a greater improvement in the AR patients in the product arm versus the sham arm.

There were only 10 patients with severe nasal congestion at baseline. This subgroup demonstrated a greater improvement in the nasal congestion sub-score with the product versus sham.

Summary of the Assessment of Benefit-Risk
There were no serious AEs, or SAEs reported during the clinical study. An acceptable rationale was also provided for the MCID. The study showed a statistically significant difference between the product arm and sham arm that exceeds the MCID. In addition, a greater improvement was demonstrated in the nasal congestion sub-score with use of the product compared to the sham arm in the AR, non-allergic rhinitis, severe nasal congestion, and moderate nasal congestion subgroups. Therefore, the Benefit-Risk profile is favorable.

Patient Perspectives

1) SCORE (Sonu nasal COngestion RElief) Study

Subjects reported their nasal congestion sub-score and 24-hour reflective TNSS at baseline and after their second treatment each day on the Sonu App. The nasal congestion sub score is part of the TNSS, a validated symptom severity scoring system (*Downie SR, Andersson M, Rimmer J, Leuppi JD, Xuan W, Akerlund A, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. Allergy Eur J Allergy Clin Immunol. 2004;59(4):406–14*). The nasal congestion sub-score is evaluated using a scale of 0=None, 1=Mild, 2=Moderate, or 3=Severe.

2) Sonu Usability Study

A usability study was conducted on 25 participants using the Sonu App (iOS application) and the Sonu Band. The study participants were adults, 22 years of age or older, seeking an over-the counter (OTC) treatment option for moderate to severe nasal congestion. The study was administered by an observer. No treatment was delivered to the participants. All participants were surveyed after using Sonu using a usability questionnaire. Responses the individual questions on Ease of Understanding Instructions and Ease of Use of Device are summarized in Table 11 and Table 12, respectively. All participants either strongly agreed or agreed that the instructions were

easy to follow, and Sonu was easy to use. No neutral or negative responses were noted. No observations or issues were noted by the observer in terms of the participants' ability to understand, set up and operate the App and the headband. Overall, the feedback demonstrates that the majority of subjects found Sonu easy to use and were able to follow the instructions for use without assistance or guidance from the observer.

Table 11. Ease of Understanding Instructions

1) Instructions for using the Sonu Headband are easy to follow with clear steps.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2) Sonu App instructions are well illustrated with clear and understandable graphics.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3) Sonu App was easy to understand.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
24 (96%)	1(4%)	0 (0%)	0 (0%)	0 (0%)
4) Step-by-step instructions made the Sonu App easy to operate.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
22 (88%)	3 (12%)	0 (0%)	0 (0%)	0 (0%)

Table 12. Ease of Use of Sonu

5) When I opened the Sonu package, the contents were easy to identify.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6) Sonu headband buttons and functions were easy to identify and operate.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
23 (92%)	2 (8%)	0 (0%)	0 (0%)	0 (0%)
7) I was able to wear the Sonu Headband easily.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
8) I was able to wear the Sonu Headband correctly.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
9) Sonu was easy to use.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
10) I am comfortable with using Sonu.				
Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
25 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Benefit/Risk Conclusion

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

Sonu is indicated for the relief of moderate to severe nasal congestion due to allergic and non-allergic rhinitis. Sonu is a treatment to be used at home by individuals 22 and older.

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

CONCLUSION

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

Product Code: QNT

Device Type: External mechanical stimulator for the relief of congestion

Regulation Number: 21 CFR 874.6100

Class: Class II